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DISEASES OF CHILDREN

JULY 1956

VOLUME 92 NUMBER

Treatment of Tuberculosis Meningitis Without Injections
W. P. Sweetnam and C. G. W. Sykes

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Epidemic Staphylococcal Gastroenteritis in a Newborn Nursery
Richard T. Smith

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A. M. A.
Journal of Diseases of Children

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A.M.A. Journal OF
DISEASES of CHILDREN

Editorial

During the past few months there have appeared some changes in this journal suggested by the readers to increase its usefulness. In this issue there is introduced a major change in the abstract section, more fully described at the beginning of that section. It is the opinion of the Editorial Board that more complete abstract services are now available, but that our readers will appreciate an opportunity to scan the titles of articles of pediatric interest in the leading journals and to have more complete abstracts of a few selected articles.

The Section "Correspondence" is being continued, in which columns we will be glad to publish letters relating to any point of pediatric interest.

Another departure is the reproduction of the Scientific Exhibit "Congenital Aganglionic Megacolon" by John F. Mokrohisky, M. D., and George P. Keefer, M. D., in the December, 1955, issue. It is our opinion that valuable exhibits have been prepared which have been shown to limited groups but which may be suitable for permanent reproduction in a journal of wide scope. It is our hope that photographic reprductions of these exhibits will be submitted for this section accompanied by whatever explanatory comment may be necessary.

We will be interested to hear from the readers about these changes, or to receive new suggestions for improvement of the Journal. The main purpose remains as it has always been, to provide a general pediatric journal of interest both to the practitioner and to the more academic man, for there is something of interest for all in the most abstruse paper and the research man should not lose sight of the problems of the practitioners. The success of a journal depends on whether it meets the needs of its readers. We welcome, therefore, your comments.

The Treatment of Tuberculous Meningitis Without Injections

W. P. SWEETNAM, M.D., M.R.C.P., D.P.H., D.C.H.
and
C. G. W. SYKES, M.B., D.R.C.O.G., D.C.H.
Huddersfield, England

The treatment of tuberculous meningitis has undergone a progressive review following the introduction of streptomycin and later of aminosalicylic acid (PAS) and isoniazid. Streptomycin has two main disadvantages—the need for prolonged injections and the occasional toxicity of the antibiotic. Oral isoniazid has been shown to produce adequate bacteriostatic levels in the C. S. F. (Fletcher, 1953) and to be virtually nontoxic (Medical Research Council, 1953).

Smellie (1954) has drawn attention to the pain and suffering caused to children by prolonged courses of intrathecal and intramuscular injections, and suggests, from his own experience, that intrathecal treatment can be dispensed with. Morin (1952) obtained promising results in five patients with the use of isoniazid alone, a short course of intrathecal treatment being given. Applebaum and Anderson (1954) report 7 recoveries in 10 cases treated with isoniazid or iproniazid; in 3 cases the initial therapy was administered intramuscularly. Sweetnam and Murphy (1952, 1954) treated two children with isoniazid alone by mouth, with good results. Ratner and co-workers (1953) report the recovery of one child treated solely with isoniazid by mouth. Spies and associates (1954) in a series of 13 cases claim that the results obtained with isoniazid orally as the only method of treatment were as good as those obtained with isoniazid and streptomycin.

Submitted for publication March 22, 1956.

Consultant Pediatrician (Dr. Sweetnam) and Pediatric Registrar (Dr. Sykes), The Huddersfield and Halifax Hospital Groups.

Materials and Methods

In an endeavour to compare the treatment by isoniazid alone with the more conventional form of therapy all admissions from April, 1952, to May, 1954, were treated alternatively under Regimen A or Regimen B. A total of 10 cases were treated, 5 in Group A and 5 in Group B. In every case the clinical diagnosis was confirmed by the characteristic changes in the C. S. F. (low cell count with a predominance of lymphocytes, low sugar, and high protein) and by the demonstration of the tubercle bacillus in the C. S. F. All patients were conscious on admission and were classified according to the Medical Research Council (1948). The following regimens of treatment were adopted:

Group A

1. Isoniazid by mouth in a dosage of 4 mg/lb. daily in divided doses for a year
2. Streptomycin intramuscularly 20 mg/lb. daily in 12-hourly doses for six months
3. Streptomycin intrathecally 1 mg/lb. daily for three months
4. Aminosalicylic acid 200 mg/lb. daily in divided doses for one year.

Group B

Isoniazid by mouth in a dosage of 4 mg/lb. daily in divided doses for a year

No departure was made from these rigid schedules of treatment.

Results

The Table gives brief details of the 10 patients. There were two deaths in the series, one in each group. Case 3, Group A, was in the intermediate stage. Two days after admission he had a series of severe convulsions, lapsed into coma, and died a week later. Case 10, Group B, was also

Clinical Details of Cases.

Case No.	Age, Yr.	Group	Clinical Assessment on Admission	Isolation of M. Tuberculosis	Mantoux	Other Evidence of Tuberculosis	Result
1	1½	A	Intermediate	C.S.F.+	+	Nil	Recovered
2	1½	A	Intermediate	C.S.F.+	+	Nil	Died
3	1½	A	Early	C.S.F.+	+	Military lungs	Recovered
4	1½	A	Intermediate	C.S.F.+	+	Pleural effusion	Recovered
7	6	A	Early	C.S.F.+	+	Nil	Recovered
9	10	A	Early	C.S.F.+	+	Mother sputum+	Recovered
2	6	B	Early	C.S.F.+	+	Military lungs	Recovered
4	5	B	Early	C.S.F.+	+	Nil	Recovered
6	11/12	B	Early	C.S.F.+	+	Choroidal tubercles	Recovered
8	6	B	Intermediate	C.S.F.+	+	Nil	Died
10	5	B	Intermediate	C.S.F.+	+		

an intermediate case. He responded well to treatment initially and progress was satisfactory for nearly two months when he developed an intercurrent infection. His meningeal signs returned. Streptomycin was then given in addition to isoniazid. He again responded and appeared to be progressing well when he suddenly collapsed and died. The survivors have been followed up for varying periods from the start of treatment, five for more than 3 years, two for more than 2 years, and one for 19 months.

Various factors have been used in assessing progress.

Fever.—It has been suggested that either the intrathecal irritation produced by streptomycin or the stress of repeated lumbar punctures may be responsible for prolonging fever. This was not our experience. The temperatures of all cases settled within three weeks. There was no appreciable difference between the two groups.

Constitutents of the C.S.F.—For the same reasons it has been suggested that with intrathecal treatment the C. S. F. takes longer to return to normal. This appeared to be so in this series. In those receiving intrathecal treatment (Group A) the longest period before the C. S. F. returned to normal was 40 weeks, the shortest 28 weeks, the average being 32 weeks. In Group B the shortest period was 10 weeks and the longest 24 weeks, the average being 19 weeks. C. S. F. examinations are of little assistance in assessing clinical progress. They are now being done much less frequently.

Weight.—In Group B there was a speedier return of appetite and a greater initial weight gain. From two months onward the weight gain in the two groups was broadly similar.

Neurological Complications: In Group A, Case 1 developed a mild hemiplegia. This child is able to walk and run fairly well and has some weakness of one arm. He is also mentally retarded. Two other children in Group A, cases 7 and 9, had some disturbance of equilibrium, presumably due to vestibular damage. Both these children appeared to have fully compensated for this disability by nine months. There were no neurological complications in Group B.

Comment

The number of cases in each group is too small for any concrete deductions to be made. The minimum follow-up period has been taken at 18 months as relapses after this period appear to be unusual. This has resulted in the exclusion from the present series of a further four cases, two in each group, all of whom are progressing well but have not as yet been followed up for this minimum period.

It must be emphasized that, although the cases were unselected, all were either in the early or intermediate stage. None could be classified as severe. This is probably due to the increased awareness of the importance of early diagnosis. It does appear that isoniazid alone by mouth may prove to be an effective form of therapy and certainly justifies further trial. In all cases isoniazid was given continuously for a year, a much longer period than appears usual.

The treatment under Regimen A is distressing to patient and staff. Children re-

main nervous and apprehensive throughout the long course of intrathecal and intramuscular injections. A prolonged stay in an acute ward is needed. In contrast, treatment under Regimen B could hardly be simpler. Once the children have recovered from the acute phase they are among the happiest in the ward and can be transferred to a long-stay hospital after about a month.

Summary

Ten consecutive unselected cases of tuberculous meningitis in children were treated alternatively either with a combination of streptomycin, isoniazid, and aminosalicylic acid (Group A) or with isoniazid (Group B). There were two deaths, one in each group. The eight survivors have been followed up for periods ranging from 3½ years to 19 months. All are well except one case in Group A who has a mild hemiplegia and is mentally retarded.

In this series of cases the results obtained with isoniazid by mouth as the sole method of treatment are at least as favorable as those obtained under the more orthodox treatment. Treatment with isoniazid is very much simplier. No injections are required. This is a particularly welcome feature with children.

Our thanks are due to the junior medical, nursing, and laboratory staffs of both hospital groups.

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Gallstones in Children

Report of Four Cases

DONALD P. BABBITT, M.D., Milwaukee

The occurrence of cholelithiasis in childhood is rare. However, in patients with unexplained abdominal pain or jaundice it should not be forgotten in the differential diagnosis, particularly since the accurate diagnosis by cholecystography is simple and the surgical results are excellent. The presence of jaundice is far more commonly due to hepatocellular disease in children, but the possibility of cholecystitis, with or without cholelithiasis, should be kept in mind.

Diagnosis

It may be possible to demonstrate calcified stones in the gall-bladder region by using posteroanterior, oblique, and lateral projections.

Harris and Caffey [1] reported that the results of cholecystography using iodopanoic acid (Telepaque) were excellent in children more than 11 months of age. The usual dosage of iopanoic acid (Telepaque) was 0.15 gm. per kilogram of body weight in younger children. In older children 4 to 6 tablets were given the evening before with fat-free meal followed by filming in the morning, much as the procedure is done in adults. If no gall-bladder shadow was seen, a repeat dose was given the same morning with filming in the afternoon, six to eight hours later. In infants under the age of 11 months the results were less satisfactory, but from the practical standpoint this is probably not significant because the occurrence of gallstones below the age of 11 months is extremely rare.

Submitted for publication Dec. 28, 1955.

From the Department of Radiology, Milwaukee Children's Hospital.

Iodipamide (Cholografin) sodium may be helpful in cases of nonvisualizing gall bladder or questionable common-duct stones if there is adequate liver function determined by laboratory tests (sulfobromophthalein sodium [Bromsulphalein] retention of less than 15% to 20%).

Report of Cases

CASE 1.—A white girl was admitted to the hospital at the age of 23 months for acute otitis media. An uneventful recovery ensued. At that time the laboratory findings were normal except for leucocytosis. At the age of 2 years 10 months she was again admitted, with a diagnosis of acute glomerulonephritis, from which she made a satisfactory recovery. In the course of the work-up for glomerulonephritis an excretory urogram was done which showed no abnormality except for the presence of calcific shadows in the right upper quadrant, which lay outside the confines of the kidney. Cholecystograms were done with single and double dose of iopanoic acid; both examinations showed nonvisualization of the gall bladder. The oblique and lateral projections indicated that the calcific shadows lay in the gall-bladder region, with a questionable small stone shadow in the region of the common duct. On review of the chest film done at the age of 23 months, the same calcific shadows were present but had been overlooked. The serum bilirubin direct was 0 mg.; total was 0.3 mg. The hemoglobin ranged from 11.5 to 12.6 gm. per 100 cc. The red blood cell fragility test was negative. The icterus index was 22 during the acute phase of the glomerulonephritis and four days later was 11. No clinical jaundice was noted. There had been no history of jaundice, and there was no history of jaundice in the family. At the age of 3½ years, after recovery from the acute glomerulonephritis, there was a history of frequent bouts of vomiting lasting a day, preceded by anorexia for a week or 10 days. Occasionally pain was present in the right upper quadrant, particularly after meals which contained fatty foods.

Cholecystectomy was done at the age of 3½ years. The gall bladder was small, shrunken, and thick-walled. The common duct appeared slightly

larger than normal. An operative cholangiogram was made and showed no sign of stone, obstruction, or other abnormality. Incidental appendectomy was done.

The pathological report showed a stone measuring 0.4 by 0.5 cm. in the lumen of the gall bladder. A "small amount" of white milky material was present in the gall bladder also. The fundus of the gall bladder was thickened. Diagnosis was chronic cholecystitis with cholelithiasis and acute appendicitis with pinworms.

The surgical recovery was uneventful. Follow-up after one and one-half years showed no further symptoms.

CASE 2.—Three weeks before admission to Milwaukee Children's Hospital, a 12-year-old white girl had had a shaking chill and complained of abdominal pain and headache. She was admitted to another hospital, where a diagnosis of anemia was made. Temporary improvement occurred after transfusion, and she was discharged. Several hours prior to admission to Milwaukee Children's Hospital she again had abdominal pain and vomiting. There was a history of having always been "yellow." On examination at that time there was evidence of icterus, splenomegaly, and a palpable liver, which was tender. Hematologic study showed findings characteristic of familial spherocytic anemia. Gall-bladder examination revealed impaired concentration of the contrast material and several partially calcified stones averaging 2 to 3 mm. in diameter. Splenectomy was done without complications. At the time of splenectomy the gall bladder was found to be thin-walled, soft, and pliable and contained several small, millet-seed-sized, soft stones. In view of the size of the gallstones demonstrated radiographically and surgically it was thought likely that they would pass without cholecystectomy. Therefore the gall bladder was not removed. Cholecystography was repeated one year after surgery with decubitus films and again several months later. Both cholecystograms revealed normally functioning gall bladder without stones.

In the interval between splenectomy and normal cholecystograms, a period of several months, the patient had several bouts of midepigastric pain after meals. No episodes of pain were experienced after the cholecystograms, which were normal.

Hematologic studies of two siblings and the parents revealed the presence of spherocytes in the mother's smear.

CASE 3.—A 12-year-old white boy had a diagnosis of Laennec's cirrhosis of the liver two years before the present admission, and at that time the clinical findings were typical. Jaundice and severe hepatic damage were present. The laboratory data indicated a normocytic, normochromic anemia with leucopenia, thrombocytopenia, and granulopenia. The RBC fragility test was negative. The patient was seen by a hematologist whose opinion was that the anemia was due to Laennec's cirrhosis with secondary hypersplenism and not to hemolytic anemia. Splenorenal shunt was done because of portal hypertension. A liver biopsy at that time revealed Laennec's cirrhosis. A gall-bladder examination done at the age of 12 years, using iopanoic acid, revealed the presence of multiple calcific shadows in the gall bladder. The abdomen was opened, and portal portography was done to evaluate the splenorenal shunt, and at that time a cholecystectomy was performed. Pathological examination showed 20 black, hard, irregularly shaped stones measuring 0.1 cm. to 0.4 cm. in diameter. Liver biopsy again showed Laennec's cirrhosis. Pathological diagnosis was chronic cholecystitis with cholelithiasis and Laennec's cirrhosis.

Follow-up studies show that the patient continues to have normal liver function tests but is otherwise progressing satisfactorily, in view of the presence of Laennec's cirrhosis.

CASE 4.—A 13-year-old white girl had been under treatment for many years by the orthopedic service for idiopathic scoliosis, for which a spinal fusion had been done. She was found to have calcific shadows in the right upper quadrant on routine films taken during the course of study of the scoliosis. At the age of one month she had had a Ramstedt operation for hypertrophic pyloric stenosis, with uneventful recovery. At the time the calcific shadows were seen in the right upper quadrant, additional studies were done with contrast material, which showed calcific shadows in the region of the right upper quadrant without evidence of concentration of the contrast material by the gall bladder. The study was repeated using 4 gm. of iopanoic acid (8 tablets), and again the gall bladder was not visualized. The oblique and lateral projections indicated that the calcific shadows were in the gall bladder and cystic duct. Medical history indicated that the patient had had no evidence of any food intolerance and no history of jaundice, anemia, or other abnormality. Laboratory studies on several occasions were negative. The hemoglobin ranged from 11 to 17 gm. per 100 cc. over a six-year period. No specific tests for hemolytic anemia were made.

The patient was lost to follow-up for four years but when contacted was found to have had several bouts of epigastric distress, and she gave a history of fat food intolerance. Intravenous cholangiogram with iodipamide sodium showed nonvisualization of the gall bladder, with enlargement of calcific shadows in the gall bladder but normal common duct. Cholecystectomy was done at the age of 17 years. There was evidence of chronic cholecystitis, and the lumen of the neck of the gall bladder was occupied by numerous, rather friable,

small calculi. The final diagnosis was chronic cholecystitis with cholelithiasis.

The above four cases of gallstones in children were recognized during a three-year period, from 1952 to 1955. No other cases are on record at the Milwaukee Children's Hospital. Two of the four cases were found on x-rays done for other reasons. These were the two cases without apparent hematologic abnormality.

All four of the above patients had calcific shadows in the gall-bladder region visible on the plain films. Three of the four patients had nonvisualization of the gall bladder with repeat double-dose examination. The presence of calcification of the stones indicates that cystic-duct obstruction probably had been present before the calculi were recognized. The youngest child had calcified gallstones at the age of 23 months. Of the two patients with jaundice, one had familial spherocytic anemia and one Laennec's cirrhosis. The other two had no hematologic or liver abnormality, although one of these had no specific tests for hemolytic anemia. Liver biopsy was done only on the patient with Laennec's cirrhosis.

Comment

In an excellent review of cholecystitis in children by Ulin and others in 1952,[2] a striking incidence of jaundice was noted. Up to 1952, there had been 472 cases of cholecystitis in children reported in the literature, not all of which were subsequently satisfactorily proved by pathological examination. In a series of 30 cases of pathologically proved childhood cholecystitis occurring between 1938 and 1948, there were 43.3% complicated by jaundice, 57% had cholelithiasis, and 7% had choledocholithiasis.

The high incidence of jaundice and low incidence of common-duct stones seems to be best explained by a very acute inflammatory process in the gall bladder, which in children lies quite close to the common duct. The proximity of the structures could produce intermittent common-duct obstruction. The passage of small common-duct stones could account for the jaundice, but this is less likely.

Cholelithiasis is frequently related to excessive excretion of pigments due to hemolytic anemia. The significance of this association is important, because if hemolytic anemia is present proper therapy usually consists of splenectomy followed by cholecystectomy at a second operation. In view of one of the reported cases (Case 2), if the stones are small a waiting period with repeat cholecystogram may be tried since the stones passed in this instance. In a high-grade common-duct obstruction, duct exploration may be required first. Splenectomy and common-duct exploration should not be done together because of the high risk of severe or fatal shock.[3]

Cholecystitis without cholelithiasis occurs particularly in association with acute infectious diseases such as peritonitis and meningitis.

In a report by Griffin and others,[4] it was found that the incidence of carcinoma of the gall bladder in young adults and adolescents was the same as in the older population, approximately 2%.

Cholecystic disease is a complication of more than 50% of patients having hemolytic jaundice. It does not follow that patients with cholecystic disease have a high incidence of hemolytic disease. This point is emphasized in the report of Griffin, who found that 40 patients under the age of 25 had cholecystic disease but only 2 had hemolytic disease, an incidence of 5%.

Summary

Although cholelithiasis and cholecystitis are rare in childhood, the possibility should be considered in the differential diagnosis of unexplained abdominal pain and/or jaundice. Cholelithiasis in children can be accurately diagnosed by cholecystography. The results of cholecystectomy are excellent.

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Some Observations on the Teaching of Medical Psychology in Pediatrics

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In discussing the actual teaching of medical psychology as a part of the pediatrics education, the teacher should define his aims and objectives as they pertain to the particular situation he operates in and as they may be intergrated into the over-all teaching program.

As an associate in the Department of Pediatric Psychiatry, Children's Hospital, Washington, D. C., I conduct a teaching conference once a week for one hour on clinical problems related to pediatric psychiatry. The group is made up of approximately 16 fourth-year medical students from the George Washington and Georgetown medical schools, the resident (pediatric) staff rotating through the department of psychiatry, social workers, and, occasionally, nurses. It is obvious that most of the medical students in the group will never practice pediatrices as a specific specialty. However, although the conference endeavors to integrate the past and present psychiatric training of undergraduates and residents, particularly to pediatrics, certain basic psychiatric principles and problems are discussed which are applicable to the general practice of medicine, such as the physician-patient relationship, the gathering together of data, the dynamic and genetic aspects of human behavior presented in simple descriptive terms, the patient's relationship to the family and society, and the management of less complicated emotional disturbances. Nevertheless, the major objective is to acquaint the participants with an understanding of and the methods of management of psychological problems in the sphere of interest of pediatrics. The case material is used primarily for teaching purposes in this conference. During the six weeks in which each group of students attend the conference, an attempt is made to present some of the commonest emotional problems related to pediatrics, such as emotional components in organic disease, psychosomatic disorders, feeding difficulties, disturbances of elimination, fears and phobias, mental retardation, and learning problems and school maladjustment on an emotional basis.

The case conference is an ambitious one. It endeavors to synthesize the data contained in the case which has been worked up and is presented by the students or residents. The entire activity is carried out in examining rooms and conference rooms outside of the department of psychiatry. We hope to provide the participants with a meaningful experience which aids them in developing a receptive orientation toward emotional problems. They have the opportunity to observe the practical application of theories of psychological growth and development in children as well as the role of the family and community in the emotional difficulty. They discuss the overt and covert forces which operate between the doctor and the patient. They have a chance to see children communicate their problems through symbolic language and behavior.

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They become acquainted with the unique position of the pediatrician to family life and community agencies and public-health personnel. Out of all these factors they formulate practical treatment procedures in the management of the problem. The participants are encouraged to utilize these principles and concepts in a scientific context with as much objectivity as possible through group discussion and consenus; otherwise it is felt that the material will have little meaning to them.

It is important to mention my previous relationship to the fourth-year students of the George Washington University School of Medicine, for this influences very strongly the way I participate as the group leader in the clinical conference. I taught them a course in "Introductory Medical Psychology" in the first semester of the freshman year. One of the assignments in the course was to fill out a detailed personal inventory of their lives. This inventory was kept absolutely anonymous, but the students were encouraged to answer each question with as much objectivity and forthright honesty as possible. Now, in filling out this personality inventory certain important factors were noted which seem to be of specific significance in suggesting ways to teach students that may more effectively modify their resistance to psychological phenomena. The study showed that too many of the students basically are anxious, insecure, hostile, and unreceptive to any teaching experience. It points up the need to consider the psychological organization of the student in relation to the specific material under consideration.

Out of a class of 99 first-year medical students, 50% felt that no teacher exerted a positive permanent influence on their personality, and, of these, 63% recalled a most traumatic experience they had with a teacher. As to their reaction to authority, 63% respected and accepted qualified authority, 24% did not accept authority well, and 13% rebelled or rejected it. In taking advice or criticism, only 45% could accept it if constructive and sincere, 39% usually listened with embarrassment or discomfort, and 16% rejected it or discounted it. They were asked, "How do you react if proved wrong?"; 33% said they would agree, 50% said they usually admit it but feel shaken and embarrassed, 17% said they would not admit it and would rationalize the mistake, 25% were of the conviction they were always right. Thirty-six per cent said their feelings were easily hurt, twenty-three per cent said this happened in specific situations, and forty-one per cent felt they were not easily hurt. Twenty-three per cent disliked adapting to new surroundings and twenty-two per cent stated they initially disliked it. Forty-two per cent said they liked responsibility only if they were sure of themselves; nine per cent disliked it and forty-nine liked it. Eighty-four per cent felt they had a good sense of humor. Sixty-seven considered themselves stubborn. Thirty-eight per cent had no interest in the humanities. Thirty-three per cent thought they were imaginative; forty per cent idealistic, twenty-one per cent visionary, and eighty-two per cent considered themselves basically practical.

It is apparent that many students approach new ideas wtih caution and reluctance. It also is obvious from this material that many of the students have rigid defensive personalities and feel more comfortable in the tutorial system of classical teaching, where their feelings will remain contained and safe. Nevertheless, it is suggested that for certain types of teaching, if it is carried out in a noncritical atmosphere, where humor can blunt intense anxiety, and the teaching has a practical quality to it, the students would be more receptive to the new experience. In other words, the manner in which ideas are presented may stimulate the readiness of the student to accept them. These are the principles which in part approximate the psychotherapeutic atmosphere.

Now, to get back to the clinical conference on pediatric psychiatry, it is necessary to

describe my relationship with my associates and how the teaching atmosphere is structured. I feel the relationship to one another of those doing the teaching may determine for better or worse the student's receptivity to the material. If there are any serious conflicts, either open or hidden, the anxiety may be passed on to the students and create confusion in them as to their position in the program. Fortunately, the climate of the hospital and the teaching staff is receptive to the problems of psychiatric teaching, which at best is so highly charged with anxiety. We know each other well, and have had previous experience in teaching medical students. All of us have been trained to work as a clinic team in relation to child psychiatry, and we have a psychoanalytically oriented approach to the problems of human behavior. Through initial discussions group we formulated our objectives in each phase of the teaching operation so that we know where we stand in relation to each other. Likewise, a monthly group discussion gives all of us a chance to examine problems as they arise and to evaluate our own role in the teaching program. It also provides us with an opportunity to express and become better aware of our own anxieties which could interfere with the program, and this has been of great help.

Before scrutinizing the teaching experience, I want to describe a typical case conference. This case could have been about enuresis, sleep disturbance, psychogenic vomiting, and the like, but happened to be this one when the material was put together. The following material, obtained from the mother, was presented by a fourth-year student in the general conference room. Before the conference started, I got a note from the social worker stating that the student was very apprehensive. As the student presented the material, his voice barely carried and he obviously was unsure of himself. The problem was that of a 9-year-old Negro boy with school maladjustment and emotional immaturity. The mother was reluctant to talk about her child. She complained that she had trouble getting him to go to school. During the first year of school, the mother carried him in her arms to school each day. She has continued to take the child to school and has asked to have him excused 15 minutes earlier than the other children. She felt that his trouble was due to the crowded neighborhood they lived in, in a housing authority. The other children, whom she considered dirty and ill-mannered, would not play with him and beat him up. The mother tried to invite other children into the home but was compelled to wash their hands before giving them a cookie.

The father is 62 years old and previously married. The mother is 40 years old and has been married for 20 years. He is disgusted with his wife becauses she babies the patient. She thinks of her husband as an old grouch. There is one other child, a boy, 14 months younger than the patient. The mother felt that with the birth of her children her freedom was taken away. Since then, the parents have slept in separate bedrooms. The mother will tolerate no fighting between the brothers and favors the younger one.

The development history showed that the child sat up at 4 months, walked at 9 months, talked early, and did not soil himself after he was 2 years old. However, the mother had great difficulty weaning him from the bottle. He refused solid food; so the mother puréed all food and gave it to him in a bottle until he was 4 years old, at which time she took the bottle away against his will. The student presenting the material contacted the teacher and was told that the patient could not play with other boys, held himself aloof, wanted to be near the teacher during the play period, was an average student, and was brought to school by his mother.

Another fourth-year student saw the child, who sat by his mother until she told him to go with the doctor. Upon entering the playroom, he immediately walked to

the books, saying that he had a set of Golden Books, that his favorite story was Cinderella, and that the fairy godmother his favorite character. He kept himself busy straightening up the room, so that it was in better order than when he came in. Seeing a ball, he said that he had five bats and two balls at home but would rather play on the merry-go-round with two girls. He knew he could beat up his brother, but his brother licks him most of the time. He wanted to do things with his father, such as hike and fish, but he never did. Joe Louis was his favorite, and he liked the "Cavalcade of Sports." The youngster stopped the interview by saying that he was going with his mother to hear the Chicago Symphony Orcestra at 2 p.m. When the child got to his mother he moved into the background.

As the part of the history obtained from the mother was presented, derisive laughter occurred among the groups, indicating anxiety. It was clear that unless the group got a clear picture of the child's difficulties with the mother and her problem in her home, the material would have little meaning to them. After several questions by the students in which they asked for a clarification of some of the data, I posed a question to the group. I wondered whether the child's relationship to the mother, his inability to let go of her, was based on genuine love or hateful feelings. All the group stared at me for a few moments. Then a woman medical student said she thought it was based on hateful feelings. They were invited to express their feelings, but they held back waiting for me. I gestured to one to express his opinion. He replied "Oh, no, you are trying to trap me." I said, "Then perhaps all of you could feel the same feelings toward me for posing this question as this little boy could feel toward his mother, that is, you could feel unsure of your relationship to me. If you express your real feelings, I may not like it, so you think." All of them laughed. The student to whom I asked the question then spoke up and said, "He couldn't like a mother who keeps carrying him to school." With that, a student in the back of the room said, "I saw this child in the Allergy Clinic, and he was frightened when he got his shot. I was furious with the mother, the way she treated him. She humiliated him and yelled at him." The student who presented the case now spoke up and said, "She was 200 pounds; she was huge." And the entire group again laughed. I sort of mused that it was valuable to recognize our own feelings, since they could give us a clue as to how the child felt. Nevertheless, I wondered about the danger of feeling hostile to the mother. Another student spoke up and said it would prevent us from seeing the mother's problem with the boy and the boy's problem with the mother. We couldn't work with the mother if we felt hostile toward her. Here we observed the operation of countertransference forces, which, if they persisted in the clinical or teaching situation, would prevent constructive communication in discussing and analyzing the problem.

During this hour the group brought up many other problems. They reviewed, step by step, the child's behavior in the playroom and discussed his wish to have his dependency needs met and his inability to relate himself to a male because he was preoccupied with an intense involvement with his mother. They felt she blocked his free expression of his aggressive drives. There was a discussion centered about the child carrying his behavior into his community and school relationships, and one student said he thought the boys beat him up because he was trying to hold on to something they had to give up. Again there was laughter. One student wondered how much of the child's behavior was greed and how much of it was disappointment in his mother. This led to the discussion of the weaning process, the birth of his brother, and the fact that he may have held on to the bottle as an expression of his disappointment and anger. Another student was sympathetic to the father and felt it must be

difficult for a 62-year-old man to really share in life with his boys. Attention again was drawn by me to the mother's problems and her anxiety. The group expressed the feeling that the mother must be a very dependent person herself because of her reaction to the birth of her children and the difference in age between herself and her husband and because she handled her disappointments with resentment and bitterness toward life. I then asked, "Well, if a mother felt that her own dependency needs were not met and she could not directly express her anger, how would she feel toward her child if he thought that his dependency needs were not met and he felt hostile." One student said, she couldn't help him because she couldn't help herself with her own problems. They were asked how such a child would handle his feeling of disappointment and different statements were made, such as, by being a feeding problem, not wanting to leave his mother, clutch her to give him what he wants.

Now all of this is of little value unless the group is able to see a practical way to deal with this material. So, I suggested that in the light of what we know about this material, if they were in practice in some small town what would they do. One said he would want to discuss the problem with the mother, her dissatisfactions which prevented her from letting go of the boy. Another said he would want to talk to her about the boy to help her understand his disappointment. Suddenly some one said, "But you can't leave out the father; he should be seen, too." Another student commented that if he were angry at the mother he would refer her to the local public health nurse.

It is obvious that this type of a teaching group relationship is a complex, multipurpose educational experience for all concerned. The contrast is great between the tutorial system of education and the self-directed group activity in which all are active participants. In the group structure the orientation, nevertheless, is educational and confined to understanding the meaning of human growth and behavior patterns and finding practical ways of dealing with related problems as they arise. The principle is one in which the students feel a self-directed need to seek for solutions with an interchange of ideas among all of the members of the group, who are closely identified with each other and support each other in the teaching group experience.

The climate established by the group leader or teacher will define the direction of and the value of the learning experience. It is necessary to consider ways to utilize to advantage the students' defenses related to the learning experience. This includes the management of the anxiety so that the experience is not too painful to the student and the hostility which causes regressive behavior in a group. Both interfere with the receptivity of the group to the learning process. The group-teaching situation appears to have many advantages in the teaching of pediatric psychiatry. The members of the group as a whole show less restraint in discussing the material. By contagion, one expresses an idea and it is reinforced or clarified as it is picked up and spread to the others. The group also tends to lessen the intolerance many students have to such anxiety-laden material as is touched upon in pediatric psychiatry. It also permits the expression and clarification of contradictory ideas existing side by side, even in the same person.

A brief comment is needed as to the function of the teacher in this phase of the teaching experience. Certainly he needs an adequate and relatively comfortable background of experience and knowledge related to pediatric psychiatry. Otherwise, his own anxiety may lead to the disintegration of the group action. He must have clear in his own mind what the objectives and goals are. This does not imply that he is prepared beforehand to direct the group action. I feel if one comes to the conference prepared as to what will be discussed, then the group will not work out their own problems

related to the material and will not be able to synthesize the material as their own. Group stability must be maintained. At times, one of the students may react excessively to the material or toward others in the group. Permitting group consensus regarding the problem usually contains such a student. But it is important that the problem raised be adequately disposed of so that the student's self-esteem is not shattered. Deep-seated problems in a member of the group may be exposed in such a teaching situation, and they require quick neutralization by sticking to the clinical problems at hand so that the group remains intact instead of becoming involved in a personal problem.

It is difficult to scientifically assess at this point this type of teaching in pediatric psychiatry. Aside from attempting to achieve the main objectives already mentioned, it is hoped that the students become more comfortable, more tolerant, and more understanding of themselves and their patients. Also, that they achieve a broader horizon upon which to envisage human behavior, rather than within the narrow confines of an organic orientation to the practice of medicine.

Congenital Methemoglobinemia in the Newborn Period

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Congenital or idiopathic methemoglobinemia is an inborn error of metabolism which may or may not be familial. In this condition 20% to 40% of the hemoglobin is in the methemoglobin form, in contrast to the normal values of 0.01% to 1.8%* The enzyme system which regulates the balance between hemoglobin containing iron in the ferrous state and methemoglobin containing iron in the ferric state is disturbed.† A lavender blue cyanosis is the most marked clinical feature of the disease and usually is present in varying degrees from infancy. The administration of reducing substances, such as methylene blue or ascorbic acid, decreases the amount of methemoglobin. Hence, this feature is of value in differentiating between methemoglobinemia and cyanotic congenital heart disease.[6] The two cases presented demonstrate the importance of early diagnosis for the prevention of hypoxia and death. These are the first recorded cases of congenital methemoglobinemia diagnosed and treated in the newborn period.

Report of Cases

Inasmuch as both cases are brothers, first attention will be given to the family history. A review of the family background failed to reveal any previous instance of congenital or idiopathic cyanosis. The parents and the two older siblings of the patients had normal methemoglobin values. The father's blood type was found to be B(CDe/cDE) K Fy^{a}p, and the mother's, A (cDe/cDe) k Fy^{a}p.‡ She never had been given a transfusion or injection of whole blood. There was no history of drug or contaminated-water ingestion.

Case 1.—The first boy was the product of a normal nine-month pregnancy and spontaneous four-hour labor. The birth weight was 6 lb. The infant cried immediately after birth, had a normal pinkish hue, and had no respiratory distress. Eight hours later he choked and turned a deep blue color, which cyanotic state persisted despite oxygen, high humidity, and antibiotic administration. He was examined by the attending physicians, Capt. Sheldon C. Siegel and Capt. Irving R. Fox, who found no abnormalities other than the cyanosis. There was no respiratory distress, no cardiac murmur or abnormal neurological signs, e.g., depression, absence of the Moro reflex, or convulsions. Rooting and sucking reflexes were normal. On the third day, while the infant was still cyanotic and in a high-oxygen environment, moderate jaundice was noted, which persisted for two days and then faded rapidly. While he was jaundiced he regurgitated several feedings without becoming dehydrated. Blood culture showed no growth. The hemoglobin was 16.1 gm/100 ml., red blood cell count was 5,510,000/milliliter, white cell count 12,000/milliliter, and platelet count was 220,000/milliliter. No nucleated red blood cells were seen on peripheral blood smear. The blood type was B (CDe/cDE) K Fy^{a}p. Urinalysis, chest roentgenogram, and electrocardiogram were within normal limits.

On the 16th day of life the methemoglobin value was 6.44 gm/100 ml.§ and the hemoglobin

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* References 1 and 2.

† References 3-5.

‡ Serotyping was carried out by Lieut. Col. Joseph H. Akeroyd (MSC), Asst. Chief, Dept. of Hematology, Army Medical Service Graduate School, Walter Reed Army Medical Center, Washington, D. C.

§ Methemoglobin determinations were done by the spectrophotometric method described by Evelyn and Malloy[7] and by Hawk, Oser, and Summerson.[8] The tests were performed by Miss Addelia Peterson, M. T., Supervisory Chemist, Chemistry Dept., Fourth Army Area Laboratory, Fort Sam Houston, Texas.

was 13.9 gm/100 ml. (46% of the hemoglobin was methemoglobin). On the 18th day of life, 0.45 ml. (1.5 mg/kilogram of body weight) of a 1% solution of methylene blue was given intravenously, and within 20 minutes a dramatic change from cyanosis to normal color occurred. The methemoglobin level after treatment was 0.46 gm/100 ml., while the hemoglobin value remained the same. Consequently, oxygen administration was discontinued. On the 20th day of life cyanosis returned to a mild degree. Treatment with 150 mg. of ascorbic acid a day was begun at this time. On the 23d day the methemoglobin level was 2.44 gm/100 ml. The infant was discharged from the nursery on a regimen of 300 mg. of ascorbic acid per day. While the infant was at home, the cyanosis varied from slight to moderate and was noted by the parents to increase with crying. At the age of one month a second dose of intravenous methylene blue was administered with the same effect as previously seen, namely, a change in color and a reduction of the methemoglobin value from 1.8 to 0.22 gm/100 ml.

At the age of 2 months, while the infant was still receiving 300 mg. of vitamin C per day, the methemoglobin value was 2.25 and the hemoglobin 9.6 gm/100 ml. His head control was poor. Gain in height and weight was normal.

At age 3 months a third dose of intravenous methylene blue was given, after which the methemoglobin value was 0.045 gm/100 ml. Cyanosis remained slight to moderate. At age 6 months the vitamin C was discontinued, but the cyanosis deepened and the methemoglobin value rose to 5.5 gm/100 ml., with a hemoglobin of 11.6 gm/100 ml. After one month of ascorbic acid administration (300 mg/day) with no change in his condition, a fourth intravenous dose of methylene blue (1.15 ml.) was given, with dramatic improvement in his color. Two weeks later, while the infant was still receiving ascorbic acid, the methemoglobin value was 1.35 and the hemoglobin 11.5 gm/100 ml.

An oral suspension of methylene blue was tried, but the resulting vomiting and excoriated buttocks were severe enough that we discontinued its use.

At age 14 months the methemoglobin level was 2.87 gm., with hemoglobin 11 gm/100 ml.

Motor development continued to be slow. By age 7 months, he still did not hold his head well, nor could he sit up, even with support. He could, however, roll over both ways by this time.

By age one year, he was babbling and could reach for and play with objects. He responded well to auditory stimuli. At age 14 months he could "patty cake." When last examined, at age 16 months, he still could not sit alone and his head control was improved but still poor. His reflexes were hyperactive bilaterally. There was no evidence of athetosis, rigidity, or spasticity, and at no time had convulsions occurred.

Case 2.—The second boy was born 11 months after Case 1, following a normal nine-month pregnancy and a spontaneous five-hour labor. Birth weight was 7 lb. He cried spontaneously. Marked cyanosis was noted immediately after birth. The cord blood was dark chocolate brown. Respirations were 86 per minute. The attending physician, Capt. Harris L. Smith, was aware of the family history, and therefore, at age 4 hours, he gave the infant 0.6 ml. of a 1% solution of methylene blue intravenously. Since improvement was only moderate, a second 0.5 ml. dose was given, and within 25 minutes the child developed a normal pink color. Oxygen was not administered. The cord methemoglobin was 5.9 gm/100 ml. and hemoglobin 15.1 gm/100 ml. After treatment the methemoglobin value was 0.28 gm/100 ml.

At age 21 hours, in addition to the bluish tinge of his skin, moderate jaundice was noted; by the 46th hour of life the jaundice was marked. The serum bilirubin was 36 mg/100 ml. His blood type was A (CDe/cDe) K fy^aP. No obvious incompatibility of blood types was apparent during the hospital stay. The later examinations by Col. Akeroyd revealed a possible Kell incompatibility, and the mother's serum was studied with 22 known red cell types, including Kell positives. No abnormal antibodies were found. Nevertheless, the diagnosis of hemolytic disease of the newborn was made. The infant had a high-pitched cry, poor rooting and sucking reflexes, and a poor Moro response. Accordingly, an exchange transfusion was carried out through a saphenous vein which was cannulated with polethylene tubing. Type O Rh-negative blood, 500 ml., was given with 10 ml. of Witebsky's anti-A and anti-B substance. The serum bilirubin was 24.8 mg/100 ml. following the exchange transfusion. Accordingly, at 58 hours of life a second exchange transfusion was carried out through the same tubing, using similar blood. The bilirubin level decreased to 14.5 mg/100 ml. The pitch of the infant's cry changed from weak and high to normal, and the Moro and other reflexes became more active.

A progressive increase in jaundice and a serum bilirubin level of 27 mg/100 ml. were the indications for a third replacement transfusion, which was carried out with similar blood through the same tubing and vein as the two previous exchange transfusions. The serum bilirubin decreased to 11.2 mg/100 ml., but on the fourth day rose to 15.6; on the fifth and the seventh days it was 10.8 and 4.1 mg/100 ml., respectively. After these procedures the infant did well and on the 10th day of life was discharged from the nursery.

By the fourth week of life he was holding his

head well, was gaining weight, and appeared robust and healthy. His methemoglobin was 0.28 gm/100 ml. and hemoglobin 8.1 gm/100 ml.

Cyanosis reappeared when the child was 3 months old. His methemoglobin was 1.5 gm/100 ml. He had been receiving 100 mg. of ascorbic acid a day, which dose was increased to 300 mg/day. He has developed in a normal manner. He followed objects with his eyes and grasped toys by one month of age. By the 3 months of age he was sitting with support. When last seen, at age 5 months, he was beginning to sit alone. His methemoglobin value was 2.42 and his hemoglobin value was 10.8 gm/100 ml.

Comment

The diagnosis of congenital or idiopathic methemoglobinemia was established in these two children first by the identification of the typical spectral band of methemoglobin at 630μ. This band disappeared immediately after the addition of two to three drops of potassium cyanide, thus differentiating it from sulfhemoglobin, which has a spectral band at 618μ that remains fixed after the addition of potassium cyanide.[9]

Secondly, the abnormally high blood methemoglobin level was reduced by both intravenous methylene blue and oral ascorbic acid.[10] Thirdly, there was no history of exposure to substances that can cause methemoglobinemia, such as contaminated well water,[11] aniline dye in diapers,‖ phenytoin,[14] or coal tar.[15] The clinical course of each infant was typical, as is indicated by the fact that methemoglobinemia has persisted though modified in degree by ascorbic acid and methylene blue.

The first generally accepted instance of congenital methemoglobinemia was reported by Francois, of Belgium, in 1844.¶ Since that time over 100 cases have been reported.#

Körver[22] has presented the youngest recorded case to date, in which the diagnosis was established by the age of 2 months. He also made, in retrospect, the diagnosis of congenital methemoglobinemia in the two older siblings of his patient. They died in the newborn period, presumably from the anoxia caused by this condition.

Baltzan and Sugarman,[23] Coudonis,[17] and Baikie and Valtis[20] have described the genetic background of several families with this disorder. Harris,[24] Baikie and Valtis,[20] and Coudonis[17] considered this to be a recessive trait, although Baltzan and Sugarman suggest that it is a dominant one.

Although incompatible in the Kell blood-group system, the mother's serum contained no abnormal antibodies to these antigens when tested six weeks after the birth of Case 2. It may be conjectured that hemolysis follows methylene blue administration, but this situation has not been reported.[25] Furthermore, repeated treatment of these infants with methylene blue did not produce a hemolytic crisis. Insofar as is known, methemoglobinemia has not occurred as part of the symptomatology of erythroblastosis fetalis, nor, according to Clark and Morrissey,[26] are elevated methemoglobin values found as a result of hemolysis. It should be mentioned that the indications for exchange transfusion were solely on the basis of the hyperbilirubinemia and not because of the methemoglobinemia. The treatment of Case 2 in regard to the hyperbilirubinemia follows the recommendations of Allen and Diamond,[27] that the serum bilirubin should be kept below 20 mg/100 ml. in the first days of life if kernicterus is to be prevented. Not only was the laboratory finding of hyperbilirubinemia present, but also the clinical findings of neurological depression. The post-exchange-transfusion motor and mental development of this child has been satisfactory.

The motor development of the first case has not been normal, but rather, markedly retarded. The occurrence of severe hyperbilirubinemia in the second infant suggests that the jaundice of the first infant

‖ References 12 and 13.

¶ Francois: Cas de cyanose congénitale sans cause apparente, Bull. Acad. roy. méd. Belgique 4:698, 1944-1845; cited by Sievers and Ryon.[16]

References 5, 6, and 17-22.

may not have been physiologic. However, the lack of the signs of kernicterus, e.g., deafness, opisthotonus, and athetosis, suggest that lack of oxygen from too prolonged a period of hypermethemoglobinemia may have been the important cause of his retardation. Worster-Drought, White, and Sargent [19] have described three instances of methemoglobinemia in older children who also had mental deficiency. They asserted that the degree of methemoglobinemia was not enough to cause the retardation seen by them. In view of the findings of this report and that of Körver, hypoxia in the neonatal period may have been severe enough to cause the retardation seen by the authors. Körver has demonstrated that even death can occur in infancy from this disease, presumably due to anoxia from the displacement of hemoglobin by the inert methemoglobin.

The early diagnosis of this metabolic defect is important, not merely to differentiate this illness from congenital heart disease and other causes of cyanosis, but also to prevent the hypoxia that may lead to death or mental and motor retardation.

Summary

Two siblings with congenital methemoglobinemia are described. The first one was treated on the 18th day of life and the second by the 4th hour of life. No comparable cases were found in a review of the literature. Both infants have required methylene blue and ascorbic acid therapy. The first child has demonstrated marked motor retardation, probably the result of hypoxia rather than hyperbilirubinemia. Despite severe hyperbilirubinemia requiring three exchange transfusions, the second child has been normal in growth and development. The importance of early diagnosis in the prevention of death or motor retardation from hypoxia is discussed.

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Penicillin V Treatment of Beta-Hemolytic Streptococcal Infections in Children

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Introduction

In this report we wish to present the results of the treatment with penicillin V (phenoxymethyl penicillin) of 110 cases of β-hemolytic streptococcal infections in children. This preparation, although discovered in this country in 1947 and used abroad clinically for several years, first became available for clinical trial in the United States in the spring of 1955. Unlike other penicillin salts, its aqueous solution is relatively stable in the acid secretion of the gastric juice. Consequently it passes through the stomach with little change and shows better absorption from the intestinal tract than is found in other preparations of penicillin.[1]

Methods

All cases were examined by one of us, and a throat culture which grew β-hemolytic streptococci was obtained prior to or at the onset of treatment. In a moderate number of children the culture was repeated within a few days of the beginning of therapy. At the end of three weeks almost all the patients visited our office where they were reexamined. At this time the throat was again cultured, the urine was examined, and blood was taken for a sedimentation rate by the micromethod of Landau.[2] Approximately three weeks later, or about six weeks from the start of therapy, a third throat culture was obtained.

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If the child was well and the culture negative at the end of this period, he was classified as "cured." If he became ill and had a positive throat culture for hemolytic streptococci up to 60 days after initial therapy he was classified as a "recurrence." If he remained well but the throat culture remained positive or became positive later, he was classified as a "carrier." In either of the last two circumstances the period of observation was concluded and therapy usually was reinstituted.

If the child was seen in the home the throat culture was obtained by a sterile swab which was immediately placed in a rubber-stoppered tube containing a small amount of infusion broth. This was swabbed and streaked on a sheep-blood agar plate on return to the office and incubated for approximately 15 hours. If the child was seen in the office the swab was inoculated directly on the blood agar plate. The organisms were isolated in pure culture on blood agar slants and sent to Dr. Harry Feldman, of Syracuse University, Syracuse, N. Y., who performed groupings and typings.[3]

The penicillin V was dispensed in tablets of 200,000 units (125 mg.). Thirty tablets were given each patient regardless of age, with instructions to take one in the morning upon awakening, one at 2 p.m., and one at bedtime. For the younger children the tablets were frequently crushed and mixed with fruit, jelly, or sugar. The parents did not report much difficulty in administration.

Material

All children were seen in the private pediatric practice of the authors during the six-month period ending Oct. 1, 1955. The sex distribution of the children was about equal, and the ages of the majority were between 4 and 9 years (Table 1). When the drug became available to us, we were engaged in a study of other therapeutic agents, consequently those who received penicillin V frequently were suffering from recurrent attacks of streptococcal disease which had previously been treated by some other penicillin product. Thus the patients in which penicillin V was first tried did not represent a true cross section of this type of infection in pediatric practice, but

TABLE 1.—*Age and Sex Distribution of Treated Cases*

Age, Yr.	Male	Female	Total Number	%
Under 2	0	0	0	
2	1	2	3	2.7
3	4	2	6	5.5
4	7	6	13	11.8
5	21	3	24	21.8
6	4	10	14	12.7
7	10	8	18	16.5
8	4	10	14	12.7
9	2	2	4	3.6
10	3	1	4	3.6
Over 10	5	5	10	9.1
	61	49	110	100.0

they were biased by having a larger proportion of carriers and therapeutic failures among them.

In the series there were 56 cases of streptococcal sore throat, 19 pyogenic streptococcal complications (11 cervical adenitis, 4 otitis media, and 1 each of sinusitis, peritonsilar abscess, vaginitis, and impetigo), and 35 carriers (patients not ill but with positive throat cultures).

Eighty-eight per cent of the patients with streptococcal sore throats, 80% of the "carriers," and 53% of those suffering from pyogenic infection had strongly positive cultures (3+ or 4+). The remainder were less strongly positive.

The distribution of streptococci found in these patients according to group and type is given in Table 2. In this small number the only suggestive

TABLE 2.—*The Groups and Types of β-Hemolytic Streptococcal Infections Observed in Treated Cases*

	Strep Throats		Pyogenic Infect.		Carriers		Total	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Unknown	4	7	3	17	3	9	10	9.1
Not Group A	4	7	1	5	7	20	12	10.9
Group A								
Untypable	25	45	8	42	9	25	42	38.2
Type 1	7	12	4	21	5	14	16	14.6
4	2	3	1	5	1	3	4	3.6
6	6	11	0		6	17	12	10.9
12	0	0	0		1	3	1	0.9
13	1	2	1	5	1	3	3	2.7
19	0	0	0		1	3	1	0.9
22	1	2	0		0	0	1	0.9
28	6	11	1	5	1	3	8	7.3
Total	56	100	19	100	35	100	110	100.0

difference in the streptococci found in patients in the three categories is the larger percentage of "Not Group A" among the carriers.

Results

Of the 110 patients originally treated, 4 were not followed and were excluded from the series. Of the remaining 106 patients, 6 had recurrent attacks and 17 became carriers at various periods up to 60 days after therapy (Table 3). Another child developed

TABLE 3.—*Time After Therapy that Clinical Recurrences or the Carrier State was Observed*

Days	Recurrence, No.	Carrier, No.	Total No.	Per Cent
Under 16	2	1	3	13
16-30	1	11	12	52
31-45	2	4	6	26
46-60	1	1	2	9
	6	17	23	100

acute glomerular nephritis on the eighth day. Of the remaining 82 patients, 96% were observed for more than 15 days and 82% for more than 30 days, and these were all classified as "cured."

We should like to give more data on the 23 children in whom there was bacteriological recurrence. In 5 of them the same type of Streptococcus was observed in the original and the subsequent culture, in 7 the streptococci were of different types or groups, and in 11 they were either untypable or information is lacking about one of the cultures. This would indicate that of those which were typed at least half of the therapeutic failures, where failure is measured by clinical recurrence or carrier state, were actually reinfections. It is also conceivable that some of those with infections with the same type might also have been reinfections, but there was no way of determining this point.

In all instances where the patient was clinically ill the response to therapy was that which we have come to expect from penicillin in streptococcal infections—prompt drop in temperature and rapid improvement in the state of well-being. Parodoxically, the most dramatic response was observed in the 13-year-old boy who developed acute nephritis. When first seen he had a history of sore throat and fever of 10 days previously, from which he had seemed to recover. However, his throat then had become increasingly sore to the point where he could hardly swallow. At the time of examination he had marked cervical adenitis and a huge peritonsilar abscess nearly obstructing the posterior pharynx. With some trepidation he was given penicillin V and seen the next day.

After four 200,000-unit tablets the abscess and the adenitis had receded markedly, his temperature was down, and his culture was negative. In another day, the throat appeared normal. However, eight days later he developed classical acute glomerular nephritis from which he recovered completely.

In 40 patients cultures were taken within four days after the beginning of therapy; 20 of these within 24 hours. All but one of these cultures were negative. This one was a Group A Type 6 Streptococcus that we were unable to eliminate completely by any method of therapy.

Sixty-eight sedimentation rate tests were made—usually approximately three weeks after the beginning of therapy. All but seven were normal, and three of the seven subsequently became normal. The remaining four were not repeated.

Comment and Conclusions

It is not our purpose here to discuss the relative value of penicillin V in contrast to other penicillin preparations in the treatment of β-streptococcal infections in children, since the patients as a group are not comparable to those we have studied previously. They are biased by a fairly large proportion of children which other penicillin regimens had failed to "cure." We therefore believe that the results obtained in the treatment of randomly selected patients would be at least as good as, and probably better than, our results in this series.

Since, with rare exceptions, all the antibiotics and certainly all forms of penicillin are clinically valuable in the treatment of β-hemolytic streptococcal infections, we have come to judge our results by rather harsh standards. The therapeutic agent must be able to prevent recurrence and eliminate the Streptococcus from the throat for a period of over 21 days—preferably 42 to 60 days. The frequency with which late recurrences of streptococcal infection occur suggests that the organism is often held in abeyance but not destroyed by what is considered to be an adequate method of therapy. Obviously if the organism in the second attack is of a different group or type from the first, the second attack is a reinfection. However, a second attack might be a reinfection even when the same type of Streptococcus is involved but for the purposes of our study this is considered to be a recurrence and therefore a therapeutic failure. On this basis penicillin V qualifies well as a therapeutic agent against β-hemolytic streptococcal infections in children.

As noted above, in approximately half of the cases in which the cultures became positive after therapy and in which the type and group of the original and subsequent culture were known, the second culture was of a different group or type. Applying this figure to the group of 23 known recurrences, 11 might be considered to be reinfections rather than relapses. Thus 94 cases could be considered as "cured" by penicillin V. This gives us a "cure rate" of 88.7%. In the single case of nephritis following therapy the patient had had his streptococcal infection too long before treatment for it to have been of preventive value. No cases of rheumatic fever were observed in our series.

The immediate clinical response to this drug was good, and the cultures became negative rapidly. There were no toxic reactions, and by and large the children took the tablets without trouble. Thus penicillin V given orally appears to be an excellent therapeutic agent for streptococcal infections.

Summary

One hundred ten children with streptococcal infection were treated with penicillin V. In this group the clinical response was excellent, and the cultures became negative rapidly. The over-all "cure" was approximately 90%. No toxic reactions were observed. Penicillin V is an effective drug for the treatment of streptococcal infections in children.

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The Iodized Oil (Lipiodol) Test for Fat Absorption

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Introduction

Following the use of the administration of iodized oils as a test for fat absorption, Silverman and Shirkey [1] introduced a simple modification in which a qualitative test for iodine was performed on varying dilutions of urine collected 12-18 hours following oral ingestion of iodized oil (Lipiodol). They claimed that a positive test for iodine after the ingestion of iodized oil in a dilution of 1 in 4 or greater probably excludes fibrocystic disease of the pancreas as a diagnosis. Our experience with this test was most disappointing, negative results on undiluted urine being often found even with urine of normal controls.

We therefore tried the effect of determining the urine iodine quantitatively while preserving the simplicity of the Silverman-Shirkey technique.

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Experimental Procedure

Iodized oil was administered to patients in the Children's Hospital, Winnipeg, in the manner described by Silverman and Shirkey. Samples of urine were collected before and at intervals of 6 and 12 to 18 hours after the iodized oil had been given, and the iodine content of these samples measured by the method of Alpert.[2]

Results

Table shows the results for the control group. These were patients in the Children's Hospital with diseases not associated with faulty fat absorption.

In Table 2 are shown the findings for the children with clinical evidence of dis-

TABLE 1.—*Control Group*

No.	Age	Iodized Oil Given, Ml.	Pre-Iodized-Oil Sample, Mg. I/100 Ml.	Post-Iodized-Oil Sample			
				1st		2d	
				Time	Mg. I/100 Ml.	Time	Mg. I/100 Ml.
1	12 yr.	10	29	6	188	12	217
2	3 yr.	7.5	0	6	208	18	735
3	2 ½ yr.	5	4.3	6	296	12	400
4	16 mo.	6	26	...	...	12	334
5	1 yr.	5	7	7	227	18	389
6	8 mo.	5	9	6	86	12	229
7	16 mo.	6	0	6	166	19	178
8	1 yr.	5	0	5	53	18	565
9	6 yr.	9	0	6	106	18	622
10	9 mo.	5	0	...	...	13	339
11	1 ½ yr.	5	0	...	...	12	652
12	11 mo.	5	78	9	325	18	172
13	9 mo.	5	12.5	...	...	12	621
14	3 yr.	5.5	0	8	291	17	350
15	2 yr.	10	0	6	18	13	267
16	15 wk.	5	7.2	6	387	16	325
17	15 mo.	7	3.5	7	659	12	467
18	3 ½ yr.	5.5	5.3	6	28	11	289
19	1 yr.	5	0	6	481	11	710
20	3 ½ yr.	7	0	6	549	12	661
21	9 ½ mo.	5	0	6	13	13	126
22	22 mo.	6	8.9	8	147	14	302

TABLE 2.—*Children with Clinical Evidence of Defective Fat Absorption*

Case	Age	Iodized-Oil Given, Ml.	Diagnosis	Stool Trypsin	Duodenal Juice Trypsin	Pre-Iodized-Oil Sample, Mg. I/100 Ml.	Post-Iodized-Oil Sample			
							1st		2d	
							Time	Mg. I/100 Ml.	Time	Mg. I/100 Ml.
1	8 mo.	5	Fibrocystic disease of pancreas*	+	−	34	6	15.6	12	5.4
2	3 yr.	10	Fibrocystic disease of pancreas	−	−	0	7	28	12	31
3	29 mo.	7	Fibrocystic disease; predominantly respiratory symptoms	+	+	9	6	82	12	46
4	6 mo.	5	Malnutrition; ? fibrocystic disease	+	+	0	6	46	12	98
5	6 mo.	5	Fibrocystic disease of pancreas	−		0	5	4	17	24

* Confirmed at autopsy.

ease involving defective fat absorption.

The range of iodine excretion in the control group for the first post-iodized-oil sample was 13-659 mg. (mean, 234) of iodine per 100 ml. of urine, while that for the second was 128-735 mg. (mean, 407) of iodine per 100 ml. of urine.

Table 2 shows that all the cases proved or suspected on clinical grounds showed iodine levels lower than any in the control group, the lowest values of all being obtained in the three cases, 1, 2, and 5, where the diagnosis of fibrocystic disease of the pancreas was clearly established.

Comment

In studying the degree of absorption of any substance, the ideal method is obviously, knowing the amount administered, to determine the total quantity excreted in a given time. However, to apply such a procedure in a test on young children would be to reduce its value because of the difficulties involved in collecting urine samples passed between definite times of the day, especially in a very young age group.

For this reason then single samples of urine were collected, and the results presented in this paper suggest that the usefulness of the method is still preserved.

Whatever method is used, however, the possibility exists that low results will be obtained where renal function is inefficient. So far it has been possible to study only one case of nephrosis where the preliminary samples showed a value of 10 mg. of iodine per 100 ml. of urine, and a sample collected at 12 hours gave a value of 502 mg. of iodine per 100 ml., results well within the limits found in the control series.

Conclusions

In the 22 control subjects studied, the iodine concentration of samples of urine collected 12-18 hours following the ingestion of a test dose of iodized oil ranged from 128 to 735 mg. per 100 ml.

In three cases where a diagnosis of fibrocystic disease of the pancreas was made clinically, corresponding values of 5.4, 31, and 24 were obtained. A case of fibrocystic disease with predominantly respiratory symptoms showed a value of 46, while in a case in which fibrocystic disease had been suspected but subsequent progress had made this diagnosis unlikely, a value of 98 mg. per 100 ml. was obtained.

While the fat balance test is clearly the most logical procedure to employ, its extensive use limits the ability in a hospital to keep or attract technicians in these days where alternative employment possibilities are becoming more and more attractive.

It is suggested, therefore, the proposed test could be a useful alternative. While low results are likely to be encountered in any condition where fat absorption is defective, lowest results should appear in fibrocystic disease of the pancreas.

Summary

The Silverman and Shirkey iodized oil procedure for estimating fat absorption has been modified by quantitative determination of the urinary iodine.

The iodine content of the urine of 22 normal infants in the samples collected 12-18 hours after administration of the iodized oil varied from 128-735 mg. per 100 ml. Three infants with fibrocystic disease of the pancreas excreted 5.4, 31, and 24 mg. per 100 ml., respectively, another, with fibrocystic disease with predominantly respiratory symptoms excreted 48 mg. and a child with malnutrition in whom fibrocystic disease had been excluded showed a value of 98 mg. per 100 ml. of the urine sample collected during the 12-13 hour period.

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Erythema Neonatorum

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It is the purpose of this study to describe the manifestations of the rash of erythema neonatorum in a number of newborn infants, to demonstrate the eosinophilia in the pustules, and to discuss the eosinophilia in the blood.

For many years physicians recognized the occurrence of various reactions in the neonate during his first days of extrauterine life. They were considered evidence of the newborn's functional adjustment to his new existence. They included an erythematous or papular rash, transitory edemas of the face and genitalia, a mild generalized lymphadenopathy, breast swelling and lactation, vaginal bleeding, and icterus of the newborn. Other signs, as vomiting, mucoid or loose stools, weight loss, or transitory fever, were attributed to an irritating effect of "noxious" materials in the colostrum on the unskilled gastrointestinal tract.

Lactation and vaginal bleeding are now known to result from maternal hormone stimulation. After studies of hemoglobin and excretory liver function in the neonatal period, physiological icterus neonatorum was separated from the group. Gastrointestinal disturbances are ascribed to irritation from swallowed blood and mucus and the implantation of a bacterial flora.

The erythematous rash was well known in the 18th century, according to Smellie (1752), as quoted by Finlay and Bound.[1] It was called "the red gum" in London and "the hives" in Scotland.[2] Dewees (1826) entitled it Strophulus Intertinctus stating "very few children escape this complaint."[1] At the end of the 19th and in the beginning of the 20th centuries, it was labeled erythema dyspepticum (Moro[3]), erythema papulatum (Steiner[4]), erythema toxicum neonatorum (Leiner[5]), and erythema neonatorum allergicum (Mayerhofer*).

The English physicians felt it was related to an insufficient evacuation of meconium.[2] Dewees, in America, believed it due to "an acid state of the stomach owing to feeding improper food" or "the child being kept too warmly clad."[10] However, the investigations of von Reuss,[6] Urbach,[7] and Mayerhofer found no relationship between the rash and the "dyspeptic" symptoms, as proposed by Moro and Leiner.

The remaining findings—the rash, edemas, and lymphadenopathy—were seen together with such frequency that Mayerhofer described them as a clinical entity, "allergy of the newborn."[8] He found eosinophiles in the pustules and an eosinophilia in the blood of such newborns, confirming observations by Schick (1918), who had interpreted this as an allergic phenomenon. In a study of newborns Akerren[11] stated that spleen enlargement, noted between the second and fifth days with the greatest development of the rash, should be included with the signs of allergy. Lehndorff† suggested that hypoprothrombinemia in newborns and a rare, severe anemia (at the end of the first week of life) might also be included in the syndrome.

Mayerhofer noted a similarity of "allergy of the newborn" and serum sickness (von Pirquet and Schick[14]). In his explanation of the findings he stated that protein substances passing from mother to fetus during pregnancy acted as antigens to sensitize

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* References 8 and 9.
† References 12 and 13.

the baby. The antibodies which were produced had no untoward effect because they were detoxified and excreted by the placenta. But in the newborn remaining antibodies could not be eliminated, and the reactions which developed subsequently were evidences of sensitization. Salomonsen [15] also believed the rash was "an allergic reaction, but the allergen that is responsible has so far not been identified."

Clinical Material and Methods

Seventy-five newborn infants who developed the rash were chosen at random and examined each day during their hospital stay (four to six days). Observations were made between 10 a.m. and 2 p.m., when a notation was made of any rash, its change, and its appearance as it disappeared. A system of abbreviated descriptions was used to indicate the type of rash (erythema, macules, papules, pustules), its location (face, neck, anterior and posterior chest, abdomen, back, buttocks, extremities), and its character (blotchy, peppery, very fine, rare, residual). Blood counts were performed in this time. Other examinations on morning and afternoon rounds affirmed the impression of the rapid alterations of the rash.

To obtain the total circulating eosinophile count, a methylene blue-phloxine mixture,‡ prepared freshly each day from stock filtered stains, was used as a diluent. It consisted of one drop of methylene blue in 4 cc. of phloxine to produce a purple-red sheen. A blood sample was taken from a freely flowing heel puncture into the white-blood-cell pipette and diluted as for a leucocyte count. The pipette was shaken by hand for five minutes, the stained cells counted after settling in the white cell squares of both ruled sections of a Neubauer chamber, and the average taken as the total eosinophile count. A relationship of this number to the leucocyte count/cu. mm. (which was done at the same time using 1% acetic acid as the diluent) was obtained in per cent form by dividing the first total by the second. Wright's stain was used for the differential white blood cell counts and on the smears of pustule contents.

In another group 228 consecutive newborns were followed in a similar manner. The study of these infants was done in November and December, 1952, to avoid possible confusion with the erythemas and miliaria rubra occurring in the summertime.

A simple method of care was used in the nurseries. Except for weighing and occasional aspiration, the infant was left undisturbed in a Trendelenburg position for 12 hours. Thereafter, dextrose water followed by a formula (powdered infant food [Bremil]) was offered every four hours. No oil was used on the skin. A bath with hexachlorophene (PhisoHex) was given if there was bloody material adherent to the skin or hair. Occasionally hexachlorophene produced a transitory erythema. Silver nitrate used in ophthalmic prophylaxis was not found to be the cause of the rash.[18]

‡ References 16 and 17.

Clinical Observations

Erythema neonatorum began on the face, especially the cheeks. An erythema of varying extent spread rapidly to the forehead and within a few hours extended, in a centrifugal manner, to the extremities. Its color ranged from pink to scarlet. In a few hours macules appeared in the same areas, commencing on the cheeks and spreading downwards to the body. In a few cases the erythema persisted two or three days before macules developed. In one baby the typical macular rash, with papules, occurred five days after the persistence of a brilliant generalized erythema. Macules varied from pinhead to quarter size. Not uncommonly the smallest macules appeared without any previous erythema and tended to be more scattered, fewer in number, and sharply demarcated. They were lighter in color, were ephemeral, and could easily have been overlooked. There were several instances when the macular rash had a peppered appearance resembling freckles.

When the macules were typical, they were large and dark with irregular margins which blended into the surrounding erythema or stood in sharp contrast to the unaffected skin. Usually they became confluent, and a blotchy appearance resulted. The macules blanched momentarily to the palpating finger, which also revealed them to be thickened, like urticaria. Frequently the eyelids and the periorbital tissues were puffy and, with the rash, the face had a measles-like appearance.

Within the succeeding few hours, in the most florid examples, the other parts of the body were involved in the centrifugal progression. The large irregular macules on

the trunk produced an appearance of many welts. There was more coalescence over the thorax and back than on the abdomen and buttocks. The arms and thighs were involved moderately, while the forearms, palms, legs, and soles showed little change. In the latter areas the macules were smaller and not urticarial.

If the rash began to fade at this stage, its disappearance was again centrifugal and as rapid as its original spread. Just before it was completely gone, inspection occasionally revealed very faint and tiny macules which in some instances gave a finely peppered appearance to the skin.

Where the rash persisted, papular efflorescences arose in the centers of the erythematous macules. They became distinctly elevated, were of firm consistency on palpation, and seemed to originate deeply in the skin. When the rash was pronounced, the papules soon became broader and almost plateau-like. (Leiner compared the papules to small wheals.) Initially they were pink to red, but their color quickly changed to porcelain or pale yellow within 24 hours, when they reached their maximum development. In accord with the earlier descriptions, they were located more frequently on the posterior aspect of the body and in the gluteal region. A correlation of these pressure areas with the development of papules was suggested.

Papules sometimes arose independently of any macular stage, but pustules occurred only after papules had developed. Actually they were a more circumscribed and elevated form of the papule. They were found most frequently on the back, buttocks, and abdomen, were of uniform diameter, 2-4 mm., and were gray or yellow in color. They were superficial, not as firm as the papules, and could be broken by light rubbing. Their content was pale yellow or

Fig. 1.—Top left, a blotchy irregular and confluent macular erythema is visible on the left cheek; periorbital edema is marked. Top right, the fine discrete macules to the right (abdomen) are densely packed and deeper in color over the chest (to the left in the illustration). Bottom left, a crop of papules centrally placed in areas of erythema. Bottom right, numerous pustules scattered over the entire back.

white and resembled a purulent material. Untouched, they were resorbed completely within 24-48 hours. The photographs in Figure 1 show the stages of the rash.

Both papules and pustules disappeared first from the areas least involved, remaining longer where they were in greater concentration, especially the back and the buttocks.

Microscopically, a smear of the contents of a pustule showed myriads of brilliantly staining eosinophile leucocytes, with or without a small number of neutrophile leucocytes (Fig. 2).

Bacterial cultures of pustules were not performed routinely; however, when they were done no organisms were found. Nevertheless, pustules were, and still are, commonly confused with pyodermic infection. The absence of sparseness of neutrophile leucocytes in the smear and the fact that pyoderma develops at a later time and that infectious pustules tend to become much larger [1] were evidences of the benign nature of the pustules of erythema neonatorum.

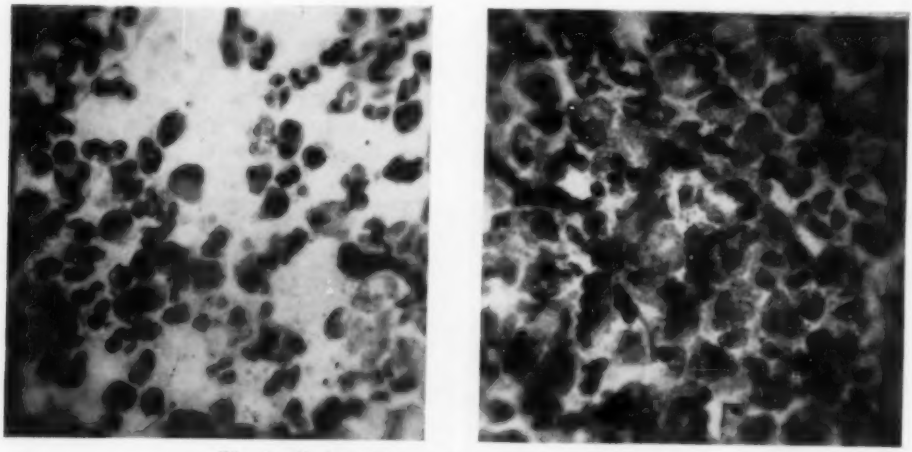

Fig. 2.—Eosinophilia seen in smears of pustule contents.

Incidence, Onset, and Disappearance of the Rash

In 16 months (1925-26), Mayerhofer followed 1115 newborns and found erythema in 46%. In our second group of 228 consecutive births (summarized in Table 1), 63 infants had no rash or only a "simple erythema," while 165 developed some kind of erythema neonatorum. Leiner described the simple erythema as occuring in the first 24-48 hours of life and attributed it to hyperemia, a cutaneous vascular response to the stimulus of the cooler external temperature. He did not include such cases in his study of erythema toxicum neonatorum. Infants with this evanescent erythema were seen in our series, but because no further change followed they were considered with the "no rash" group.

TABLE 1.—*Incidence of Erythema Neonatorum in a Group of Consecutive Newborns*

Number of babies	228
No rash or simple erythema	63 (28%)
Erythema neonatorum	165 (72%)
67 showed papules and in 19 of these pustules developed	

When the rash developed, it began on the first and second days of life in the great majority. Table 2 presents these data and compares them with Mayerhofer's findings. Table 3 shows the duration of the rash in our series. Its short course was the result of the swift progress of the macular erythema.

TABLE 2.—*Day of Onset of the Rash*

Day of Life	Per Cent of Cases: This Study	Per Cent of Cases: Mayerhofer Series
First	42	3
Second	43	30
Third	10	48
Fourth	3.9	15

TABLE 3.—*Duration of the Rash*

Days	Per Cent of Cases: This Study	Per Cent of Cases: Mayerhofer Series
1	28	12
2	32	34
3	22	31
4	11	12
5	4	11
6	1	

When the infants were followed for longer periods, Mayerhofer saw recurrences, within 5 to 11 days after the original rash, in up to 11% of the babies. We saw only a few recurrences (4.6%) because of the short hospital stay of our newborns. This rash was sparse, lighter in color, and remained for only 1 or 2 days.

The Eosinophilia

In 305 newborns (all cases in Groups 1 and 2) 225 total eosinophile and white blood cell counts were done. These counts were distributed largely over the first four days of life and represented each stage of the rash as well as cases with no rash. The total eosinophiles varied from 0 to 2000 and the leucocytes from 1000 to 50,300. Because of the wide range in figures, it was apparent that a relationship of eosinophiles to white blood cells would be necessary before any significance of the numbers could be appreciated. Each case was grouped according to the stage the rash had progressed. The precentage of eosinophiles to white blood cells was determined by simple division. The mean of the collected per cents was then plotted as ordinates and the day of life as abscissae. The graph is shown in Figure 3. Infants with the pustular form had a greater eosinophilia than those without a rash, while smaller differences were found in the papular and macular types; Table 4 summarizes the statistical validity of the findings.

The differential white blood cell counts invariably showed smaller percentages of

TABLE 4.—*Values for P (Chance Probability) for Differences in Per Cent Means for the Forms of the Rash Using Fisher's Table for T*

	First Day	Second Day	Third Day
Pustules vs. no rash	0.02	Less than 1 in 100	Less than 1 in 100
Papules vs. no rash	0.2 Not significant	0.02	0.1
Macules vs. no rash	0.6 Not significant	0.2 Not significant	0.6 Not significant

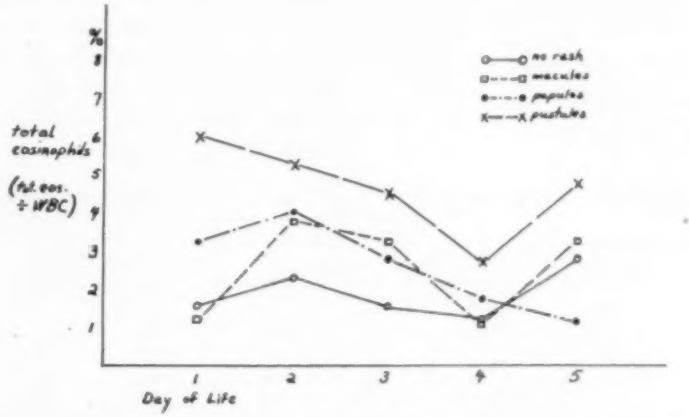

Fig. 3.—A comparison of the means of the per cents for total eosinophiles in different forms of the rash and in cases with no rash.

eosinophiles than the method described, despite the fact that 200 cells were counted.

Comment

The total eosinophile count in the newborn is known to be greater than in the adult. Also, there may be wide variation in number from one infant to another.[19] Successive counts in the first hours and days show an early rise with a progressive diminution toward the end of the first week.§ Explanations for the changes have been offered. Lippman[19] inferred that the peak at 30 hours might reflect increased production of eosinophiles because by this time the number of leucocytes had declined. The hemoconcentration following loss of body water in the first days may be another cause. Recent investigations attributed the variations to differences in adrenocortical function in newborns.‖ Support for this hypothesis was obtained from the low number of positive responses in the Thorn test[21]; however, other data ¶ were not in agreement.

One explanation for the increase in eosinophiles was clearly evident from this study: Those infants who developed pustules had significant eosinophilia compared with babies with no rash; this difference diminished when the allergic skin response was milder (papules or macules).

When the averages of total eosinophiles from cases in both groups of our patients were compared with those of Lippman's study, a similarity of the pattern of fall and rise in the first hours of life was noted (Table 5). Since we have shown that the eosinophile count is related to the rash of erythema neonatorum, it is not unlikely that the wide eosinophile range reported in the literature for newborn infants was derived in the past from inclusion of cases of erythema neonatorum. The graph in Figure 3 shows the lower total eosinophile percentages in cases without a rash.

The pathogenesis of the rash is probably due to specific sensitization of the baby to a maternal protein substance passed across the placenta. The fetus is made allergic to this substance in a similar way as every human being can be sensitized to horse serum by injection of horse serum. This sensitization has no influence upon the development of other allergic features (in the atopic person) like eczema, hayfever, or asthma in later life. Antibodies produced in the fetus are excreted by the placenta; but because the newborn is without this protection the antibodies can combine with the remaining antigen to cause the rash. The degree of its development must be modified by other factors. The resemblance to serum sickness—the facial and genital edema; the urticarial macules and wheal-like papules (Leiner); the significant blood eosinophilia, especially seen in pustular instances; the mild lymphadenopathy (Mayerhofer), and the splenomegaly (Akerran)—lends support to a hypothesis of an allergic mechanism as the cause of the rash.

§ References 19 and 20.
‖ References 20 and 21.
¶ References 22-25.

TABLE 5.—*Comparison of Average Total Eosinophile and Leucocyte Counts from the Investigation of Lippman* with Figures from this Study*

	Lippman's Study			This Study		
Age	Average WBC	Average Eos.	% Eos.	Average WBC	Average Eos.	% Eos.
½ hr.	16,600	356	2.2			
6 hr.	21,000	272	1.4	27,400	581	3.2
12 hr.	22,500	330	1.2	26,400	341	1.1
18 hr.	21,200	410	2.0	24,800	580	2.0
24 hr.	17,500	371	2.2	20,800	717	3.7
30 hr.	17,600	525	3.0	21,000	743	3.5
36 hr.	15,400	462	3.0	17,300	776	4.4
48 hr.	11,300	416	3.7	14,700	636	4.4
5 days	9,500	221	2.3			

* Lippman,[19] Tables 4 and 13.

Summary

The appearance of the rash of erythema neonatorum as it progressed through erythema, macules, papules, and pustules is described. There was an abundance of eosinophiles in the pustules, bacteria were absent from cultures, and a significant blood eosinophilia was found in our cases by comparison with infants without rash.

The presence of erythema neonatorum is given as an explanation for the wide range of eosinophiles reported for the newborn.

There is reason to believe the rash is of allergic nature of similar origin as serum sickness.

21-57 78th St.

Dr. Sidi Wasser assisted in this study. Statistical work was verified by Mr. R. Wayne and Mr. J. Black.

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Larval Granulomatosis (Visceral Larva Migrans)

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In the last decade a new clinical entity has been described in infants and young children which is characterized by a persistent high eosinophilia in the peripheral blood and bone marrow, associated with eosinophlic granulomata in the liver. Considerable speculation existed in regard to the etiology of this syndrome, but most authors agreed that the pathologic process probably represented hypersensitivity. The specific antigen was not identified in the majority of cases reported in the literature, but pollens, bacteria, and drugs were suspected. Only in five instances * were the causative agents actually determined. Nematode larvae had invaded the liver. In two cases † the offending larva was assumed to be that of Ascaris lumbricoides, but Beaver and his associates,[3] after reviewing the illustrations, identified them as Toxocara (the ascarid of dogs and cats). The larva in the third case [3] was diagnosed as that of Toxocara canis. Although Milburn and Ernst [5] could not identify specifically the larva found in the liver biopsy of the fourth case, they believed it to be that of T. canis on the basis of its diameter and length. Brill [4] identified a larva of Toxocara in a nodule of the pleura.

Beaver and his associates [3] were the first to prove experimentally that larvae of nematodes naturally adapted to hosts other than man could remain immature in the human host for a long time and could cause the manifestations of this syndrome. T. canis is probably the most important offender among the roundworms of animals with which man comes in contact. The actual animal host, however, was not demonstrated in any of the documented cases.

It is the purpose of this paper to report two additional cases of larval granulomatosis (visceral larva migrans, visceral toxocariasis). In one, a nematode larva identified as that of T. canis was found in the liver biopsy specimen; the embryonated eggs were found in the dirt ingested by the child, and the adult Toxocara was recovered in the cat, a pet of the patient's family. In the other, a larva of Toxocara was recovered from a biopsy specimen of the liver, which was studded with granulomata.

CASE 1.—A 2½-year-old white boy was admitted to the Pediatric Service of the Jefferson Medical College Hospital on Oct. 15, 1953. He had been admitted to another hospital for elective circumcision. When routine studies of the peripheral blood revealed a moderately severe anemia and 64% eosinophiles, circumcision was deferred and the child was referred to this hospital for further studies and diagnosis.

The medical history revealed that the patient had been in reasonably good health with the exception of a few minor respiratory infections. His nutrition was said to be poor, since he refused most solid foods and subsisted chiefly on milk and soups. He was never an energetic child and required 15 to 17 hours of sleep a day. The parents had noticed a paleness which had gradually increased during the past four months.

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* References 1-5.

† References 1 and 2.

Questioning elicited the fact that the family possessed three pets—a male puppy and two kittens, and the child was known to have ingested large quantities of dirt for the previous six months. Oddly enough, he was seen to ingest dirt more frequently in areas preferred by the cats for defecation. These areas included an unpaved garage floor, a back yard play space, and the dirt floor corner of the basement of the house.

The family history was noncontributory, although the father was said to have hay fever.

The physical examination on admission showed a pallid irritable malnourished 2½-year-old white boy in no apparent distress. His temperature was 101.2 F. The only abnormal findings were the presence of a few shotty cervical nodes and a soft, Grade 1, systolic murmur best audible at the apex. There was no hepatomegaly or splenomegaly, and the lung fields were clear on percussion and auscultation.

Laboratory studies revealed a hemoglobin content of 6.0 gm/100 ml., an erythrocyte count of 3,740,000/cu. mm., and a leucocyte count of 22,000/cu. mm., with 55% eosinophiles. The erythrocyte sedimentation rate was 12 mm. in one hour (Wintrobe, corrected). The cephalin flocculation test was 3+ in 48 hours, and the thymol turbidity, 8.0 units. The total serum protein was 5.72 gm. (A/G ratio, 4:02:1.7). Results of the Wassermann, tuberculin, heterophile antibody, and serum bilirubin tests were normal. Urinalyses were within normal limits. Skin and precipitin tests for trichinosis were negative. Roentgenograms of the lungs were interpreted as normal. An aspiration of the sternal bone marrow showed marked eosinophilic hyperplasia but no abnormal cells.

Examination of fecal specimens, utilizing the flotation technique with zinc sulfate solutions with a specific gravity of 1.180 and 1.240, revealed no parasites. Fecal specimens from the parents and an older brother also were negative for parasites.

Peripheral blood studies performed on the parents' blood were interpreted as normal. A 12% eosinophile count was disclosed in the examination of the peripheral blood of the older brother.

Samples of soil were collected for microscopic examination from the garage floor, the back yard play space, the dirt floor corner of the basement, and from the back yard of the child's aunt, a neighbor of the patient. The soil samples were examined directly in saline suspension and after flotation with zinc sulfate solutions of S. G. 1.240. The high specific gravity was selected because ascaris eggs vary in their buoyancy within the range 1.110 to 1.130.[6] The soil from the garage floor yielded approximately 5 embryonated eggs of Toxocara per gram of soil; the back yard play space, 4 eggs, and the basement corner, 12 eggs per gram of soil. In addition, numerous filariform hookworm larvae were seen. No eggs or larvae were found in the soil samples from the aunt's yard.

Larval granulomatosis was suspected, and a laparotomy was performed on Oct. 27, 1953, after the patient's anemia had been corrected by blood transfusions. A right paramedian incision was made for adequate visualization of as much surface of the liver as possible. The liver was found of normal size, color, and consistency. Situated on the diaphragmatic surface of the upper lobe were two small gray circumscribed lesions, each measuring approximately 4 mm. in diameter. One lesion was excised, and after fixation in 10% formalin the entire biopsy specimen was serially sectioned at 6μ thickness.

The microscopic examination of the sections revealed that the general architecture of the liver was well preserved. The capsule was normal, and there was no dilatation of the central veins. The portal triads showed normal-appearing biliary ducts.

The striking feature in all sections was the presence of numerous irregularly distributed foci of necrosis and inflammation. These foci were essentially of three types: (1) collections of eosinophiles in the sinusoids without specific zonal distribution; (2) granulomatous lesions consisting of eosinophiles, lymphocytes, epithelioid cells, and giant cells of the foreign-body type; (3) granulomata made up of epithelioid cells and fibrous tissue.

The three types of lesions blended into one another without sharp demarcation and appeared to represent different stages of the same inflammatory process.

The foci of necrosis were conspicuous only in areas rich in eosinophiles. The latter appeared to lie within the sinusoidal lumens, compressing the Kupffer cells and producing pressure atrophy of the liver cells, some of which had disappeared completely. The liver cells in the center of the lesion were necrotic, while those at the periphery were well preserved. The Kupffer cells surrounding the areas of eosinophilic infiltration and granulomatous response protruded into the sinusoidal spaces, in some places obstructing them completely. The largest focus of eosinophiles measured 6 mm. in diameter.

In the sections one well-preserved roundworm was found which had the characteristics of a larva of Toxocara. It was specifically identified as that of T. canis (the dog ascarid) by Dr. Robert L. Nichols, Department of Tropical Medicine and Public Health, Tulane University School of Medicine. The larva was lying free within a sinusoid, and the Kupffer cells in direct apposition to it appeared flat and elongated. The Kupffer cells

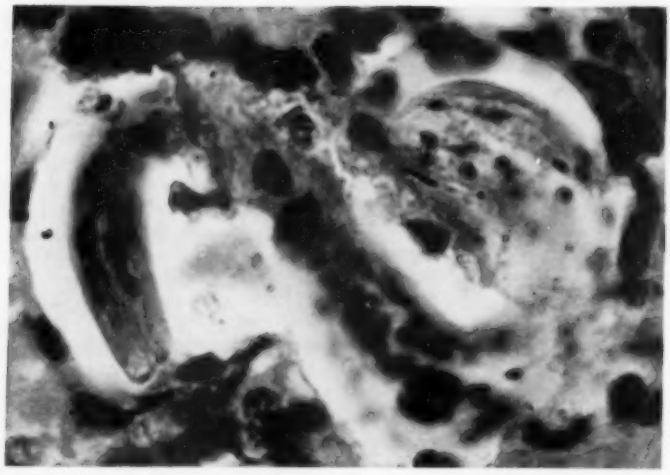

Fig. 1.—Anterior end of T. canis in section of liver biopsy specimen obtained by laparotomy; reduced slightly from mag. × 1100.

proximal and distal to the larva, on the other hand, were markedly swollen. The larva was surrounded by a loose infiltration of eosinophiles, the liver cells in these adjacent areas being well preserved. Eosinophilic granulomata were seen at a distance of approximately 1 mm., areas of necrosis and autolysis being completely absent in the tissue close to the larva. The farther the granulomata were away from the larva the more fibrous they were, suggesting that they were older, along the path of the larva.

Cultures of the biopsied material were negative for bacteria and fungi.

The stools of the puppy and the two kittens were collected and examined directly in saline suspensions and by centrifugal flotation with zinc sulfate solutions of S. G. 1.180 and 1.240. In the specimen from the puppy, eggs of hookworm and Trichocephalus vulpis (the dog whipworm) were found; in the stool of one kitten eggs of hookworm, and in the other kitten eggs of ascarids. This cat was killed. Fifteen adult Toxocara and five Dipyllidium caninum organisms were recovered from the small intestine. Eight of the Toxocara organisms were identified as T. canis and two as T. cati; the species of the other five were not determined.

No specific therapy was instituted, and soon after laparotomy the patient was discharged to be followed as an outpatient. His pica disappeared, and his appetite and general behavior were said to be excellent. Nine months after discharge the patient was free of symptoms and physical examination revealed no abnormalities. At this time his total leucocyte count was 18,000/cu. mm., with 78% eosinophiles.

On Feb. 28, 1956, sixteen months after discharge, he was still asymptomatic and his physical examination essentially negative. He had gained 15½ lb. and was of good color and extremely active. The total leucocyte count was 32,000/cu. mm., with 37% eosinophiles.

Case 2.—A 2-year-old Negro boy was admitted to the Pediatric Service of the Jefferson Medical College Hospital on June 6, 1955, for investigation of a persistent high eosinophilia in his peripheral blood. On Nov. 29, 1954, he had been admitted to another hospital with the chief complaints of fever, anorexia, fatigue, and generalized shotty lymphadenopathy.

The past medical history revealed that the patient was in reasonably good health but was subject to frequent colds. His appetite was said to be fairly good until several weeks prior to the first hospital admission. He sat alone at 1 year of age; walked alone at 18 months, and was attempting to talk at 23 months. The father was said to have asthma, but otherwise the family history was noncontributory.

Physical examination on his first hospital admission was not remarkable except for the presence of slight pharyngeal and tonsillar injection and shotty discrete cervical and inguinal lymphadenopathy. Peripheral blood studies revealed a mild anemia and a leucocyte count of 32,300/cu. mm. with 75% eosinophiles. Roentgen studies of the chest were reported as normal. Repeated examinations of the patient's fecal specimens were negative for parasites. The total serum protein was 7.6 gm. (A/G ratio, 4.2:3.4). Skin and precipitin tests for trichinosis were negative.

Direct questioning disclosed that the patient had pica and was known to have ingested dog and/or cat feces on a number of occasions.

On the basis of the high eosinophilia and the history of pica a tentative diagnosis of larval

granulomatosis (visceral larva migrans) was made. He was treated with acetylsalicylic acid, tetracycline, and ferrous sulfate, with some slight clinical improvement. The patient was discharged from the referring hospital on Dec. 11, 1954, and followed in their outpatient clinic for the next few months. Since there was no further improvement and the diagnosis not definitely established, the patient was referred to the Pediatric Service of the Jefferson Medical College Hospital for further study.

Upon admission, June 6, 1955, the physical examination revealed a small fairly well-nourished and somewhat pale 2-year-old Negro boy in no apparent distress. He was somewhat dull but cooperative. His temperature was 100.2 F. There was slight pallor of the conjunctivae and the buccal mucous membranes. The cervical, axillary, and inguinal lymph nodes were slightly enlarged but not tender. The liver was palpable 4 cm. below the costal margin. There was no splenomegaly, and the heart and lungs were normal. A fine papulosquamous rash was present over the cheeks, arms, and legs.

Laboratory studies revealed a hemoglobin content of 8.8 gm/100 ml. and a leucocyte count of 19,650/cu. mm., with 57% eosinophiles. The erythrocyte sedimentation rate was 20 mm. in one hour (Wintrobe, corrected). Urinalyses were normal. Results of the tuberculin, heterophile antibody, Wassermann, serum bilirubin, and thymol-turbidity tests were normal. The total serum protein was 7.85 gm. (A/G ratio, 3.5:4.3). Electrophoretic analysis of the serum proteins revealed hypergammaglobulinemia.

Examination of fecal specimens with zinc sulfate solutions of 1.180 and 1.240 specific gravity revealed no parasites.

An electroencephalographic tracing on June 11, 1955, was interpreted as showing depressed activity over the left frontotemporoparietal area. Psychological examination indicated that the patient's I. Q. was approximately 71.

Larval granulomatosis was suspected, and a laparotomy was performed on June 24, 1955. A right paramedian incision was made, and the liver was exposed. The liver was enlarged to about 4 cm. below the right costal margin and was studded with numerous grayish-white and reddish nodules. The largest nodule was probably not more than 7 mm. and the smallest was about 2 mm. in diameter. The nodules were firm and rubbery. A large nodule located on the free margin of the medial portion of the right lobe of the liver was excised, as was a smaller more reddish-appearing nodule located on the medial portion of the left lobe of the liver. It was felt the smaller lesion might represent a more recent stage of the disease and that two biopsy specimens might increase the probability of demonstrating the larva. Both specimens were fixed in 10% formalin, and each was serially sectioned at 6μ thickness.

Microscopic examination of the serial sections from the larger nodule showed numerous irregularly distributed foci of necrosis and inflammation but failed to disclose a larva. The histologic picture of the serial sections of the smaller biopsied lesion was similar to that observed in the specimen obtained in Case 1. In one section the tail portion of a larva was seen lying free in a sinusoid. Although the portion was not large enough to permit specific identification, Drs. P. C. Beaver (Tulane) and R. Nichols identified it generically as probably Toxocara. At the level most distant from the tip of the tail the diameter was 14μ; at the anus, 11μ. The distance from anus to the tip of the

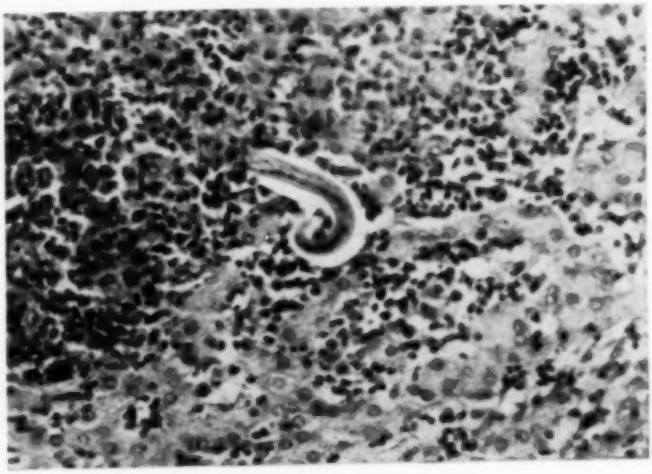

Fig. 2 (Case 2).—Posterior end of larva of Toxocara; × 250.

tail was 26μ. Cuticular annulations were visible posteriorly to the anus. The intestine was of the seven-cell type with no lumen. Characteristic basophilic granules were present in intestinal cells.

The patient's postoperative convalescence was complicated by a bacterial wound infection which slowly responded to tetracycline (Achromycin) therapy. His appetite and general behavior were much improved, but the hepatomegaly and shotty lymphadenopathy persisted. One month after the laparotomy he was free of symptoms; however, peripheral blood studies at the time of discharge still revealed a leucocyte count of 20,100/cu. mm., with 47% eosinophiles. Subsequent to discharge the patient was placed in a foster home in another state and contact was lost.

Comment

In comparing the two histories with previously reported cases of larval granulomatosis (visceral larva migrans), it is evident that many points of similarity exist. Both patients were under 3 years of age, and in each a history of dirt-eating and contact with puppies and kittens was elicited. Features in common also included a benign asymptomatic course, chronic persistent leucocytosis with moderate to severe eosinophilia in the peripheral blood, and liver biopsy findings of eosinophilic granulomatous lesions.

Although mild to moderate hepatic enlargement is usually present and has been found in 13 of 15 cases reported, there was no detectable hepatomegaly in Case 1. The liver was palpable 3 fingerbreadths below the costal cage in Case 2.

Electrophorectic analysis of the serum proteins in one patient (Case 2) revealed hypergammaglobulinemia and an increase in total globulin, but the total serum proteins as well as the albumin/globulin ratio were normal in the other case. Hyperglobulinemia is almost a constant finding and was present in 10 of 11 cases in which these determinations were made.

Eggs of Toxocara were not found in repeated examinations of fecal specimens from either patient, and this has been true in all cases studied to date. Although larvae hatch from the ingested eggs, maturity is not reached and the life cycle is not completed in man, an abnormal host. Behrer [2] recovered Ascaris eggs in one of several stool specimens from his patient, but this probably represented a concomitant infection.

Exploratory laparotomy and liver biopsy were performed in both our patients, and in each instance the liver surface showed grayish-white nodules or plaques varying in size from a few to 7 mm. The liver in Case 2 was studded with these lesions, whereas only two small circumscribed lesions were visible at laparotomy in Case 1. Microscopic examination of sections from excised lesions of each case revealed eosinophilic granulomatous lesions. Larvae of Toxocara were identified in sections of liver biopsy specimens from both patients.

No specific treatment was instituted in our first patient, who has remained free of symptoms but still exhibited eosinophilia in the peripheral blood 16 months later. A course of 1-diethylcarbamyl-4-methylpiperazine dihydrogen citrate (Hetrazan) therapy in the second patient, given six months prior to admission to the pediatric service, had no noticeable influence on the course of his disease. Case reports in the literature indicate that treatment with hexylresorcinol, Hetrazan, arsenicals, antihistamines, or cortisone has not proved to be effective.

The abnormal electroencephalographic tracing obtained in the second patient may or may not be related to damage by Toxocara larvae. The child's premature birth and history of retarded early development preclude speculation that would incriminate the larvae of Toxocara. It is of interest to note, however, that convulsions have been reported in two patients with the syndrome [5] and larvae of Toxocara have been found in the human brain at autopsy. ‡ Larvae in large numbers have also been found in the brains of mice experimentally infected with Toxocara eggs.[8] Electroencephalographic tracings are therefore warranted in patients with this syndrome.

‡ References 7 and 9.

Pathogenesis

On the basis of previously published reports and the two cases presented in this paper, the pathogenesis of this syndrome appears to be as follows:

The normal hosts of T. canis are dogs and cats. The eggs are passed in their excrement and thus contaminate the soil. In moist soil the eggs become embryonated in a few weeks, depending on the temperature and moisture, and then are infective upon ingestion. When dogs or cats ingest such embryonated eggs, the larvae hatch in the small intestine and migrate through blood or lymph channels to the liver and lungs, whence they reach the bronchial tree and trachea. Larvae, when swallowed again, mature into adults in the small intestine of these animals. The life cycle, however, is not completed in man, who is an abnormal host. In man, larvae hatching from ingested embryonated Toxocara eggs can penetrate the mucosa of the small intestine and reach the liver, lungs, or other organs, but they remain larvae, without succeeding in the completion of the cycle. They appear to migrate aimlessly through the tissues, leaving behind a tissue reaction, the allergic, eosinophilic granulomata. Smith and Beaver [8] have given experimental evidence that the larvae can remain alive for a year or more. This explains the number of eosinophilic granulomata and the persistence of hepatomegaly and accompanying eosinophilia even though the actual number of larvae may have been small. The total number of larvae and their localization in the tissues coupled with the individual patient's response account for the varied clinical manifestations.

Epidemiology

Dogs and cats are domestic animals, and few puppies and kittens ever escape infection with Toxocara. The eggs passed are not immediately infective, and so playing with these household pets and immediate accidental ingestion by way of contaminated fingers is not the route of infections as in the case of Echinococcus.

Feces of dogs and cats may be buried by beetles when they have access to them, but otherwise they are not usually disposed of in a sanitary manner. In general, the source of infection is dirt containing embryonated eggs, and the mode of infection is dirt-eating, a habit chiefly of infants and young children under 3 years of age. It is also conceivable that accidental ingestion may occur in older children and adults.

Dogs prefer or are trained to defecate outside the home; cats do not always display such preference. Thus, T. canis eggs passed by dogs are less likely to be ingested than those passed by cats. The kitten was found infected in one of our cases and appears to be the more important reservoir host. The absence of dogs was noted in the case histories of some previous reports, but the actual host was not identified. Environmental studies in the second case were inconclusive, since the infection probably occurred many months earlier. A high eosinophilia was already present six and one-half months prior to admission here. The examination of the soil at this time revealed numerous Toxocara eggs.

Smith and Beaver [8] emphasized the potential hazard of dogs and cats as housepets. They recommended deworming of puppies and kittens every few weeks. This, however, has not been veterinary practice, since immunity develops eventually and older animals then remain free. With early eradication of Toxocara, it is possible that older dogs and cats may also acquire the infection. It would seem advisable to deworm pet dogs and cats regardless of their ages.

While the number of reported cases of larval granulomatosis is very small, undoubtedly many more cases actually occur. The number probably will remain small as long as liver biopsy by laparotomy is the only means of specific diagnosis. With the advent of a reliable test such as a serologic test, not perfected yet, this disease entity will be found to be a significant health problem wherever man lives in close contact with dogs and cats.

Terminology

The term "visceral larva migrans" was chosen by Beaver and co-workers [3] for this disease to denote the aimless migration through human viscera of larvae of certain roundworms for which man is not the definitive host. It connotes that this condition is the visceral counterpart to "cutaneous larva migrans" (creeping eruption). While "visceral larva migrans" is adequate from the parasitological point of view, the term "larval granulomatosis' is proposed as the counterpart to "creeping eruption." It seems more in line with pathological terminology.

Summary and Conclusions

Two cases of "visceral larva migrans" with positive identification of Toxocara larvae in liver biopsy specimens from both are presented.

The actual animal host, a pet kitten which harbored the adult Toxocara, was incriminated in one of the cases.

The pathogenesis and epidemiology of the syndrome is discussed, and the term "larval granulomatosis" is proposed as a counterpart to "visceral larva migrans."

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Mongolism and Acute Leukemia

A Report of Four Cases

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Brewster and Cannon reported the first case of Mongolism associated with acquired leukemia in an 11-month-old "predominantly white" boy in 1930.[1] Since that time no further cases have been published, although there have been three instances of Mongolism in the 21 well-documented reports of congenital leukemia.* Of the 255 children in whom the diagnosis of Mongolism was made at Duke University Hospital in the 25-year period ending December, 1955, there were 4 who developed leukemia. The incidence is much higher than in the general population of leukemics and is reported in the hope that it may help in the general ultimate understanding of leukemia.

Report of Cases

CASE 1.—A 10-year-old white girl was first admitted to Duke Hospital in December, 1951, for evaluation and treatment of acute leukemia. The child had been diagnosed as a Mongoloid at the age of 6 weeks by her family physician. This had been confirmed at Johns Hopkins Hospital at 2 years of age, when the diagnosis of a congenital heart malformation was also made. She was apparently well until three and a half months prior to admission, when she developed a sore throat and a low-grade afternoon fever. These symptoms did not respond to sulfonamide and antibiotic therapy. One month later her gums began to bleed and a generalized purpuric rash developed She was hospitalized for four weeks in Charlotte, N. C., and treated with transfusions and corticotropin (ACTH). After discharge the child did remarkably well until two weeks prior to admission, when she once again began spiking an afternoon temperature of 104 F. Her condition slowly worsened, with falling hemoglobin and rising white cell count until the time of admission.

Past history revealed the slow development consistent with Mongolism. Physical examination revealed an obese 10-year-old white girl with a typical Mongoloid facies. The eyes were slanted and set wide apart with prominent epicanthal folds. The pupils were not abnormal. A punctate hemorrhage was visible in the left lateral fundus. The bridge of the nose was flattened, and the left naris was occluded by old blood. The lungs were clear to percussion and auscultation. The heart was enlarged to the anterior axillary line, with a Grade 3 systolic murmur maximal in the third left interspace at the sternal border. The liver was palpable 5 cm. below the right and the spleen was felt 5 cm. below the left costal margin. Numerous petechiae were scattered over the trunk and extremities, with some ecchymotic areas. The hands were short and spade-like, with transverse palmar markings. The feet were short and broad, with moderate separation of the great and second toes. The left wrist, knee, and ankle were extremely tender and showed marked limitation of motion. Generalized lymphadenopathy with nodes ranging from 0.3 to 0.5 cm. was present.

Laboratory studies on admission revealed the hemoglobin to be 6.5 gm. per 100 cc., with a red blood cell count of 2,460,000 and a packed cell volume of 22%. The white cell count was 295,500, with a differential count of 2% segmented neutrophiles and 98% lymphoblasts. The platelet count was 29,520, and there was a reticulocytosis of 0.9%. A bone marrow specimen was extremely cellular; consisting almost entirely of lymphoblasts. The urinalysis was within normal limits. The serological test for syphilis and the intradermal 1:1000 tuberculin test were negative.

The child was started on corticotropin therapy and given three transfusions. On the 12th hospital day she was discharged on maintenance cortisone with the following hemogram: hemoglobin 8.1 gm. per 100 cc., red blood cell count 3,040,000, white blood cell count 1250, with a differential count consisting of 18 segmented neutrophiles, 5 nonsegmented neutrophiles, 70 lymphocytes, 4 lymphoblasts, 3 monocytes, and 25 nucleated red blood cells per 100 white cells. The platelets were still markedly decreased, but the reticulocyte count had risen to 3.3%. Four weeks after discharge, during which time the youngster appeared to be

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* References 2-4.

in good health, she became febrile in the afternoon. One week later she again developed bleeding from the gums, purpuric lesions, and abdominal pain associated with dyspnea. On readmission the hemoglobin had dropped to 4.5 gm. per 100 cc., with a packed cell volume of 14%. The white cell count had risen to 135,000, and 96 early lymphocytic forms with 4 lymphoblasts were seen on the differential count. On the second hospital day she developed bilateral retinal hemorrhages. A third course of corticotropin was begun. On the sixth hospital day the child was transferred to a hospital near her home at the mother's request.

Case 2.—A 4-year-old white boy was admitted to Duke Hospital in August, 1952, with a history of easy bruising for six to eight months, two episodes of grossly bloody diarrhea two months prior to admission, and a constant upper respiratory tract infection associated with pallor, weakness, lethargy, and fever of two to three months' duration.

Past history disclosed the typical slow development of Mongolism. Physical examination revealed a typical Mongoloid facies, spade hands, and increased space between the great and second toes. The conjunctivae were pale but clear. A serosanguinous discharge was present in both nostrils. Encrusted blood and fresh bleeding lesions were present on the lips. The lungs were clear. The heart was enlarged to the midaxillary line with a Grade 2 systolic murmur along the left sternal border. The liver was palpable 7 cm. below the right and the spleen 5 cm. below the left costal margin. There was no generalized lymphadenopathy or skin lesions.

Initial laboratory studies showed a hemoglobin of 3.5 gm. per 100 cc., with a red blood cell count of 1,400,000 and a packed cell volume of 12.5%. The white cell count was 41,700, with approximately 80% myeloblasts in the differential count. There was a marked decrease in platelets, and the reticulocyte count was 1.4%. A bone marrow study showed the normal cellular elements to be almost entirely replaced by early and "blast" forms of the myeloid series. There was a marked decrease in erythroid activity. Urinalysis was essentially normal. The serological test for syphilis and the intradermal tuberculin 1:1000 were both negative.

Combined aminopterin and corticotropin therapy was started. In addition the child received two blood transfusions. Despite a dramatic decrease in the size of the liver and spleen and a pronounced drop in the total white blood cell count, the child's course was progressively downhill. He developed many purpuric lesions and died quietly on the 17th hospital day.

Case 3.—A 3-year-old white girl admitted to Duke Hospital in November, 1953, with a history of prolonged anemia. The child received her first transfusion at 8 months of age. Her diet had been composed entirely of milk. The child was diagnosed as a Mongoloid at that time and treated with thyroid hormone without any improvement. When she was 2 years old, she was again noted to be anemic and was treated vigorously with iron, vitamin B_{12}, and liver extract. Despite this therapy and three transfusions, the anemia persisted. Past history disclosed the slow development typical of Mongolism.

Physical examination revealed a pallid child with obvious Mongoloid characteristics. No abnormality of the eyes, ears, nose, or throat was noted. The lungs were clear. The heart was enlarged to the left, and a Grade 2 systolic murmur was maximal at the apex. The liver was palpable 3 fingerbreadths below the right and spleen 4 fingerbreadths below the left costal margin. There was generalized lymphadenopathy. The extremities were moderately flaccid. Her hands were short and stubby with abnormal palmar creases, and there was webbing between the second and third toes.

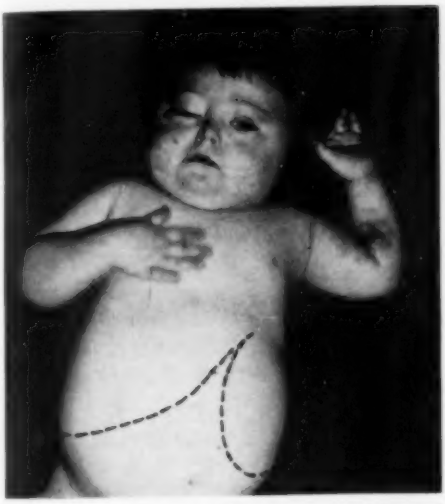
Laboratory studies revealed a hemoglobin of 2 gm. per 100 cc. with a red blood cell count of 1,060,000. The white blood cell count was 18,050, with a differential count of 5 segmented neutrophiles, 1 nonsegmented neutrophile, 57 lymphocytes, 32 promyelocytes, and 5 myeloblasts per 100 white cells. The platelets were scarce, and the reticulocyte count 1%. An attempt at a bone marrow aspiration was technically unsatisfactory. Urinalysis was within normal limits. The serological test for syphilis and the tuberculin patch test were negative.

The child was treated with cortisone, receiving one dose of aminopterin at time of discharge, nine days after admission. A report from her local hospital stated only that the child was admitted and died two weeks after discharge.

Case 4.—A baby girl was first in the Duke private diagnostic clinic at 16 months of age for confirmation of the diagnosis of Mongolism. At that time a routine hemoglobin was 12.6 gm. per 100 cc. At the age of 2 years she was admitted to the inpatient department with a history of some moderate bleeding from the vagina of four day's duration. Past history revealed typical slow development of Mongolism.

Physical examination revealed an irritable 2-year-old white girl with many Mongoloid characteristics. The other positive findings consisted of (1) liver palpable 1 cm. below the right costal margin, (2) spleen palpable 3 cm. below the left costal margin, and (3) scattered petechiae and ecchymoses over the entire body. There were no abnormal cardiac findings and no generalized lymphadenopathy (Figure).

Laboratory studies revealed a hemoglobin of 9.8



Case 4. Note the enlargement of liver and spleen, ecchymoses, and Mongoloid characteristics of face and hands.

gm. per 100 cc. and a red blood cell count of 3,690,000. The white blood cell count was 11,900, with a differential formula consisting of 22% segmented neutrophiles, 10% nonsegmented neutrophiles, 23% small lymphocytes, 3% large lymphocytes, 2% monocytes, 6% juvenile forms, 3% promyelocytes, and 31% myeloblasts. The platelets were markedly decreased, and the reticulocyte count was 1.5%. The bone marrow consisted of almost 50% myeloblasts. Urinalysis was within normal limits. The serological test for syphilis and the intradermal 1:1000 tuberculin tests were negative.

The child was started on cortisone, with gradual improvement in the peripheral blood picture. The petechiae faded: the spleen was no longer palpable, and the liver margin was at the costal margin at the time of discharge eight days after admission. Six weeks later her hemoglobin fell precipitously. She was given two whole-blood transfusions and 6-mercaptopurine was added to her therapeutic regimen. The child did well for three months and then developed daily temperature spikes. The liver and spleen again became enlarged, and petechiae reappeared. Despite numerous transfusions and antibiotic therapy the child's course was relentlessly downhill and she died with pneumonia four and a half months after the original diagnosis was made.

Little has been recorded concerning the blood picture in Mongoloids. Lang-Brown, Lawler, and Penrose † describe the blood types of Mongoloids, their parents, and their siblings as failling within normal limits. These findings have been confirmed by Benda [7] in a study of 100 (Mongoloids. He notes only one consistent abnormality in the hemogram—that the lymphocyte count in absolute number as well as in percentage is decreased.

Despite the many descriptive articles in the world literature, the pathogenesis of the group of anomalies which comprise the syndrome of Mongolism is unknown. It is generally believed that the crucial time for the development of Mongolism lies between the sixth and ninth weeks of fetal life.[8] During this time it is suspected that a stress (physical, chemical, infectious, or a fortuitous combination of these) is placed on the developing organism and produces Mongolism. Thus mongolism affects almost every anatomic system, including the brain, heart, and skeleton, which are undergoing rapid differentiation at that time.[8] Perhaps the later development of leukemia may have similar origin. It has been observed that granulocytes are present in the seventh week of fetal life, whereas lymphoblasts are not noted till the eighth or ninth week.[9] Three of our cases as well as that reported by Brewster and Cannon are probably of the myelogenous type of leukemia. Congenital leukemias in general are also predominantly of the myelogenous form.‡ This incidence might be explained if the stress occurred just prior to the eighth or ninth week.

The high incidence of leukemia in Mongolism suggests the possibility that the stress which injures the fetus at the six- to nine-week period in Mongolism may also injure the developing bone marrow and the hematopoietic system in such a way as to result in leukemia at a later date. This leads to the speculation that leukemia in normal children may have its origin in early fetal life. These prenatal influences may either be teratological in themselves or result in an increased susceptibility to more immediate

† References 5 and 6.

‡ References 2, 4, and 10.

etiologic agents, such as virus, x-rays, or other carcinogens.

We have considered whether the connection between leukemia and Mongolism might result from undue exposure to x-rays (diagnostic), since it is well known that prolonged exposure to x-rays results in an increased incidence of leukemia.[11] However, this possibility can be entertained only in Case 1, where extensive diagnostic x-rays may have been undertaken for the study of her congenital heart disease.

Summary

Four cases of Mongolism associated with leukemia are described, making a total of eight cases. In three of these, leukemia was present at birth.

The implications of this unusual association are discussed.

Addendum

While this paper was in press, five additional instances of leukemia in young Mongoloids were reported (Krivit, W., and Good, R. A.: A. M. A. J. Dis. Child. 91:218, 1956). These observations confirm the presence of an unusual relationship between these diseases which merits additional study and clarification.

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Epidemic Staphylococcal Gastroenteritis in a Newborn Nursery

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The micro-organism responsible for the majority of infections occurring during the newborn period is the Staphylococcus. While sporadic cases of minor skin infection or the occasional occurrence of septicemia [1] due to staphylococci are observed in most newborn nurseries, the more serious clinical forms of staphylococcal disease usually occur during epidemic outbreaks. A number of such epidemics have been reported recently,* and others are known to have occurred.† During these epidemics the most frequently observed clinical manifestations have been impetigo neonatorum, acute mastitis, deep subcutaneous abcesses, omphalitis, and conjunctivitis. More serious forms of infection reported as occurring during outbreaks of staphylococcal disease have included pneumonia,‡ with empyema,§ and pyopneumothorax ‖ and generalized sepsis.¶ With the exception of the report of Lyon and Rantz,[18] gastroenteritis has not been emphasized as a primary manifestation of epidemic staphylococcal infection in the newborn infant.

Recently an outbreak of staphylococcal disease in the newborn nursery of the University of Minnesota Hospitals has been observed, which at onset presented as an unusually severe form of gastroenteritis. The following report is an account of clinical and bacteriological observations made during the course of the epidemic.

Clinical Observations

On June 22, 1954, a 2-day-old, previously healthy, infant in the newborn nursery began vomiting and during the next two days retched and vomited with increasing frequency and violence. A diagnosis of partial upper intestinal obstruction was made, and an exploratory laparotomy was performed; the patient died soon after surgery. Within 36 hours, three additional infants in the newborn nursery developed a similar life-threatening illness with severe vomiting and roentgenographic evidence of obstruction. However, because of almost simultaneous appearance of skin lesions and mild diarrhea and the results of bacteriological studies, the presence of staphylococcal disease was recognized in time to institute appropriate treatment measures. After stormy illnesses, these three infants survived.

In reviewing the events leading up to the onset of illness in the infants it became clear that three infants had developed mild diarrhea with skin lesions during the previous week. A hemolytic Staphylococcus had been isolated from two of them. Subsequent to quarantine of the nursery, four

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† Anderson, A. A., and Good, T. A., personal communication to the authors.

‡ References 10-12.

§ References 13-15.

‖ References 16 and 17.

¶ Reference 1; Good, T. A., personal communication with the authors.

additional recently admitted infants developed mild diarrhea under observation; staphylococci were isolated from three of these patients. Detailed case histories with representative roentgenographic studies are given below for the four severely ill infants. The course of the disease in the less severely ill infants is described briefly in a succeeding section, and clinical data on all of the affected infants are summarized with the bacteriological findings in Table 1. The epdemiological features of this outbreak are described in the final section and summarized in Figure 4.

TABLE 1.—*Outbreak of Staphylococcal Enteritis in a Newborn Nursery*

Summary of Clinical and Bacteriological Features in Twelve Affected Infants

Patient No.*	Clinical Features				Isolation of Coagulase-Positive Staphylococci			
	Diarrhea	Vomiting	Skin Lesions	Tetany	Skin	Feces	Nasopharynx	Umbilicus
1	Moderate	Few occasions	2 large pustules		+‡	+	+	
5	Mild							
9	Moderate		Several pustules		+			
10†		Severe	Beginning excoriation					
12	Mild							
14	Severe	Severe	Severe with exfoliation	Severe	+	+	+	+
15	Severe	Severe	Severe with exfoliation	Severe	+	§	+	+
16	Severe	Severe	Severe with exfoliation	Severe	+	+	+	+
18	Mild					+	+	
19	Mild					−	−	
20	Mild					+	+	
21	Mild					−	+	

* Number refers to the order of admission to the nursery as shown in Figure 4.
† Died.
‡ +=culture grew coagulase-positive staphylococci.
−=culture did not grow coagulase-positive staphylococci.
Blank = no culture.
§ Culture lost; Gram-positive cocci predominant flora in smears of feces.

Report of Cases

PATIENT 10 (Table 1).—A boy was born on June 20, 1954, of a full-term normal pregnancy following spontaneous labor and a nontraumatic delivery. On June 22, he began to regurgitate feedings, followed shortly by development of severer vomiting of green-colored mucoid material. He had passed meconium stools and had not vomited the breast feedings or glucose solution taken prior to this time. At that time, examination revealed that the child was slightly jaundiced and dehydrated. The abdomen was not distended, and no peristaltic sounds were heard. The baby was extremely tremorous, and the deep tendon reflexes were hyperactive, but Chvostek and Trousseau signs were negative. A weight loss of 500 gm. was recorded during the first three days of life. A flat x-ray film of the abdomen showed absence of normal gas pattern (Fig. 1A). The leucocyte count was 11,250 per cu. mm., with 34% neutrophiles and 63% lymphocytes; hemoglobin value was 18.5 gm. per 100 ml.

Further x-ray studies that day indicated that iodized oil (Lipiodol) passed slowly into the small bowel. A barium enema was negative. Subdural taps were negative. A specimen of cerebrospinal fluid was obtained under normal pressure; cell count was 2 per cubic millimeter, sugar 58 mg/100 cc., protein 20 mg/100 cc., culture sterile. At this time it was first noticed that there was slight excoriation and erythema of the face and skin folds. A single loose greenish stool was passed in the immediate preoperative period. However, on the basis of absence of gas patterning and persistent vomiting, it was decided to explore the infant, with a diagnosis of a partial upper gastrointestinal obstruction. At operation the stomach and the upper portion of the intestine appeared normal; however,

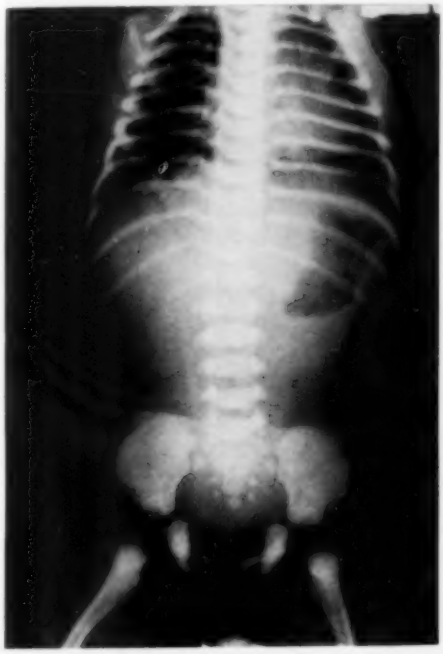

Fig. 1A.—Upright roentgenogram of Patient 10 taken 12 hours after onset of severe vomiting. Note the absence of the normal intestinal gas pattern, in spite of the presence of gas in the stomach.

the surgeon observed an unusually large amount of fluid in the peritoneal cavity. Shortly after surgery the baby's respirations became very slow and weak, and, in spite of vigorous resuscitative measures, he died.

Cultures of the blood contained no growth. Culture of the gastric fluid revealed alpha streptococci and a coagulase-positive Staphylococcus. Culture of the feces obtained by rectal swab was negative for Shigella or Salmonella but was not examined for staphylococci.

At autopsy gross examination of the gastrointestinal tract was negative. A horseshoe kidney was noted as an incidental finding. Microscopic studies revealed a marked degree of abnormal cellular activity in the mucosa of the duodenum and jejunum. Bizarre mitoses, pleomorphism of nuclei, and loss of polarity of glandular epithelium were prominent. Similar changes, less marked, were seen in the colonic epithelium.

PATIENT 16 (Table 1).—A girl was born on June 22, 1954, of a normal full-term pregnancy without complications and a spontaneous delivery. She received five glucose feedings and three breast feedings prior to the onset of illness of June 24. That day a routine newborn examination had revealed excoriation and redness of both cheeks, nose, and chin, but this was interpreted as resulting from rubbing on rough crib sheets. Shortly thereafter she began to vomit a green mucoid material and during the following day continued to vomit intermittently. Excoriation of the cheeks increased, with spread of the lesions to the neck and right arm. The temperature rose to 100 F. Vomiting became more violent on June 26, and she began to have green watery stools. An x-ray of the abdomen (Fig. 1B) showed almost total absence of the normal intestinal gas pattern at that time. This was interpreted as consistent with high intestinal obstruction. Cultures of the skin, blood, nasopharynx, and stools were taken. Leucocyte count was 6800 WBC per cu. mm., with 15% neutrophiles, 72% lymphocytes. Hemoglobin value was 12.3 gm. per 100 ml. A spinal tap was negative. A coagulase-positive Staphylococcus was isolated in almost pure culture from the nasopharynx, skin, and stool. Smears of the stools showed only Gram-positive cocci. Cultures of the blood and spinal fluid were sterile. Her clinical course is summarized in Figure 2.

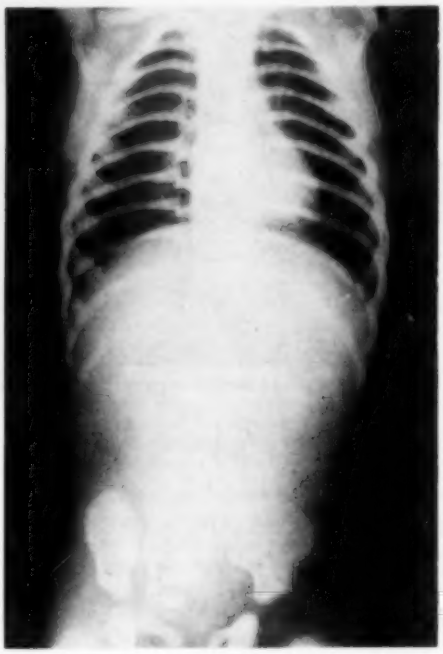

Fig. 1B.—Upright roentgenogram of Patient 16 approximately 18 hours after onset of vomiting. At this time the baby was also beginning to pass liquid green stools. Complete absence of intestinal or gastric gas shadows is clearly shown. Films taken two days later, after antibiotic treatment had been initiated, demonstrated normal amounts of gas throughout the bowel.

Fig. 1C.—Upright roentgenogram of Patient 15 taken 18 hours after birth at a time when respiratory difficulty was present but prior to development of vomiting or diarrhea. The gas pattern appears normal for an infant of this age.

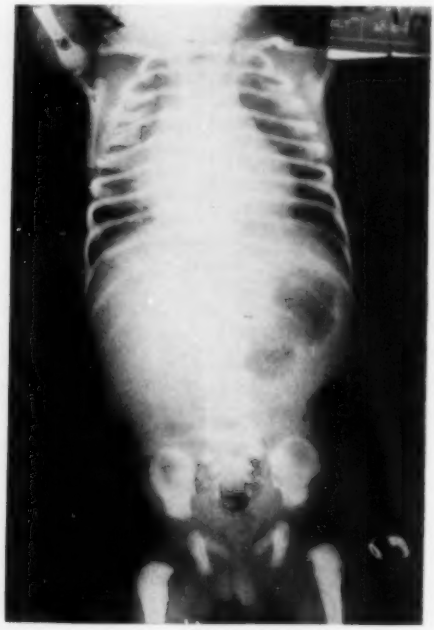

Fig. 1D.—Film taken 48 hours later, 12 hours after onset of vomiting but before diarrhea started. Note the marked decrease in intestinal gas as compared with Figure 1C.

She was started on intravenous fluids, given intravenous tetracycline 20 mg/kg/day and penicillin 1,200,000 units per day. Frequent tremors were noted within a few hours of the starting of intravenous fluids, and shortly thereafter the child was noted to lie in an opisthotonic position and develop what appeared to be severe tetany. The blood calcium level was 11.3 mg/100 cc. at that time, and she responded only temporarily to intravenously administered calcium gluconate and oxygen. Vomiting, intermittent twitching, and tetany continued. Intramuscular erythromycin, 25 mg/kg/day, was started after sensitivity studies were performed (Table 2) and continued for 10 days. On June 29, singular large bullae were seen to form over the head and extremities and soon to become confluent. Shortly thereafter exfoliation of the superficial layers of the skin over these areas, estimated to cover about 50% of the body surface, occurred. Areas of the arms and legs were completely denuded. In addition to intensive treatment with erythromycin, she was given small plasma or blood transfusions, as indicated by changes in the hemoglobin value, and neomycin ointment was applied locally to the denuded areas. Tetany continued to be manifest intermittently in spite of general improvement. She continued to regurgitate frequently for 10 days until she was given small doses of atropine; after this the symptoms ceased, and the infant began to gain weight.

Patient 14 (Table 1).—A girl was born on June 22, 1954, weighing 4350 gm., the product of a normal pregnancy and spontaneous delivery. On June 23, she began to vomit. A liquid green stool was noted on June 24. At that time she was also observed to have marked reddening and excoriation of the cheeks, nose, and chin, with redness extending down on the neck. That night intense diarrhea and severe vomiting began; she became very lethargic. Cultures of the nasopharynx, blood, stools, and skin were taken. The nose and throat cultures grew coagulase-positive staphylococci; stools grew almost pure cultures of a coagulase-positive Staphylococcus and a smear of the stool revealed Gram-positive cocci. Blood cultures showed no growth. Culture of the involved skin grew a coagulase-positive Staphylococcus. Leucocyte count was 8600 per cu. mm., with 34% neutrophiles and 56% lymphocytes. Hemoglobin value was 19.5 gm/100 ml. Intravenous fluids and intravenous tetracycline, 20 mg/kg/day, and penicillin, 1,200,000 units/day, were given initially. Neomycin ointment was applied to the skin areas. Shortly after starting therapy, she began to show convulsive movements at irregular intervals and the abdomen became distended. The blood calcium

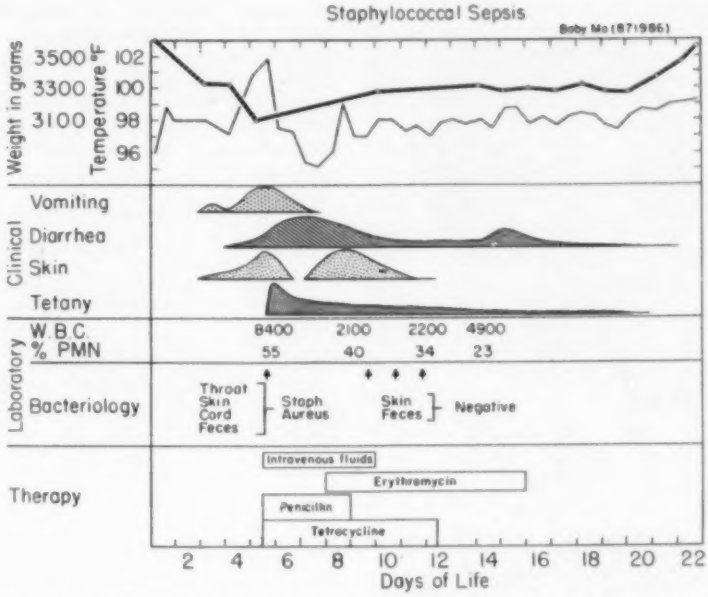

Fig. 2.—Graphic chart depicting the chronological sequence of the clinical and laboratory features of disease in Patient 16 in relation to therapy. The sequence shown is representative of that observed in each of the three severely ill surviving infants.

TABLE 2.—*Outbreak of Staphylococcal Enteritis in a Newborn Nursery: In Vitro Antibiotic Sensitivity Studies of Coagulase-Positive Staphylococci Isolated from Three Severely Ill Infants*

Patient	Source	Sensitivity, γml.			
		Penicillin	Tetracycline	Chloramphenicol	Erythromycin
16	Feces	>15.6	>62.5	15.6	1.9
14	Feces	>15.6	>62.5	7.8	1.9
15	Nasopharynx	>15.6	>62.5	7.8	1.9

level at that time was 7.3 mg/100 ml. The convulsions responded temporarily to intravenous injections of calcium gluconate. Twenty-four hours later, erythromycin was given intramuscularly, 35 mg/kg/day, on the basis of sensitivity studies of the Staphylococcus isolated from the stool (Table 2).

On June 29, large bullae were noted over the head and extremities, followed by exfoliation of the skin, eventually involving almost the entire body. A photograph of the infant after the exfoliation was well under way is shown in Figure 3. The coincidence of marked lability of body temperature control exhibited by this infant and a very warm environmental temperature resulted on one occasion in a verified elevation of body temperature to 108 F. Environmental temperature was about 100 F. Because of the exfoliation and slight oozing of the denuded surfaces, small blood transfusions were given repeatedly.

After a stormy course, the child's improvement was signalled by disappearance of the skin lesions, cessation of mild tetany, and weight gain.

PATIENT 15 (Table 1).—A premature infant boy was born on June 22, 1954, weighing 1845 gm. Delivery was accomplished by breech extraction. During the 24 hours following delivery, the infant's respirations were intermittently labored and occasional cyanosis was observed. Because of prematurity, respiratory symptoms, and the abnormal delivery, he was given 30,000 units of penicillin and 30 mg. streptomycin three times a day prophylactically.

On June 25, regurgitation after feeding was first observed, and simultaneously redness and excoriation around the umbilicus was found. The following day vomiting became severe, and he was observed to be lethargic and slightly cyanotic. X-ray examinations of the chest and abdomen in series from birth showed the presence of a normal

Fig. 3.—Photograph of Patient 14 taken 2 days after beginning of generalized exfoliation. The areas of denudation, most clearly shown here on the neck, the ear, and the posterior aspect of the shoulder, resulted from rupture of large coalescing bullae over the area approximately 24 hours earlier. The face, trunk, and proximal extremities were similarly involved, particularly in the skin folds.

abdominal gas pattern at birth and at 2 days of age but nearly absent intestinal gas on the first day of vomiting. Roentgenograms illustrating this serial change are presented in Figures 1C and 1D. On June 27, after cultures of the nasopharynx, umbilicus, and stool were taken, tetracycline, 20 mg/kg/day, was given intravenously, with intravenous fluids. Cultures of the nose and umbilicus revealed coagulase-positive staphylococci. A smear of the stool showed a predominence of Gram-positive cocci, but the culture was lost. The blood culture was sterile. On this day loose green stools were noted for the first time. A shrill cry, labored breathing, and twitching were manifest repeatedly during the 48 hours after beginning therapy. Twenty-four hours later, intramuscular erythromycin, 25 mg/kg/day, was added to the treatment regimen on the basis of sensitivity studies (Table 2). On June 28, the infant was still passing liquid green stools in profusion but was not vomiting. The abdomen appeared distended for the first time, and some twitching spells were observed. Vomiting and what appeared to be tetany recurred on June 30; the latter responded to oral administration of calcium lactate. A serum phosphorus value at that time was 7.2 mg/100 cc. Moderate exfoliation of the skin was apparent three days after starting therapy, but no bulla formation was seen. At this time the leucocyte count was 4350 with 44% neutrophiles, 52% lymphocytes.

Soon diarrhea ceased, he gained weight, and he seemed alert. He was discharged after 54 days of hospitalization weighing 2540 gm. and was doing well.

Observations

In each of these four severely ill infants abrupt onset of severe gastrointestinal symptoms was the outstanding clinical manifestation of staphylococcal infection. The initial symptom was vomiting with pronounced retching, followed shortly by the development of diarrhea. Between episodes of vomiting, the infants were apathetic and seldom cried. Roentgenograms of three of the infants revealed striking absence of the normal gas pattern. This feature was so pronounced in Patient 10 that it played an important role in the decision to explore the infant on a diagnosis of partial upper gastroinestinal obstruction. Peristaltic sounds were absent, or greatly diminished, in each of the infants; no distention of the abdomen was observed.

The skin lesions were similar in each infant. They began as apparently benign excoriations of the cheeks, chin, and nose, interpreted by various observers as resulting from the abrasive action of rough crib sheets. The appearance and extent of these lesions rapidly changed, with intense reddening of the excoriated areas and spread of the lesions down the neck to the arms and chest. On the second day of therapy, Patients 14 and 16 were observed to develop generalized bullae over the head, face, shoulders, chest, thighs, and arms. These bullae ruptured on pressure, with release of serous fluid. Nicolsky's sign was strongly positive. Apparently similar exfoliation in newborn infants has been described in the literature as Ritter's disease, epidemic form.# A very high fatality rate is recorded in the reported cases.

Although pronounced erythema of the involved areas was observed, purulent dis-

References 19 and 20.

charge, edema, or other evidences of inflammation were not evident. It is of interest in this connection that at no time during their illness did the peripheral leucocyte count in the infants exceed normal limits; however, two of the infants, Patients 14 and 15, developed leucopenia coincident with exfoliation.

The treatment program for these infants was directed toward maintenance of blood volume, restoration of fluid balance, attempts to counteract the tetanic episodes, and administration of specific antibiotics. Maintenance of blood volume was a particularly difficult problem in Patients 14 and 16 at the time when generalized exfoliation was occurring. During this critical period, repeated small transfusions of whole blood and plasma were required to maintain the infants free of evidence of hemoconcentration. The principal sources of fluid loss were the exuding denuded surfaces, diarrhea, and vomiting. However, high environmental temperature, up to 100 F, during the period of the outbreak undoubtedly contributed significantly to the large fluid losses. As a consequence, prodigious quantities of intravenous fluids were required to maintain fluid balance in these infants. These fluids were supplied as hypotonic polyionic solutions similar to those suggested by Lowe.[22]

Initial antibiotic therapy of these infants was designed to include drugs which would be effective against either an enteric pathogen or the Staphylococcus. They consisted of 1,200,000 units of penicillin per day intravenously; tetracycline, approximately 20 mg/kg/day, intravenously, and neomycin 10-75 mg/kg/day, orally. After isolation of the responsible micro-organism and completion of sensitivity studies two days later, erythromycin 35-50 mg/kg/day was given, replacing the penicillin and tetracycline. After this antibiotic was started, staphylococci could no longer be isolated from the feces.

Observations on Infants with Mild Diarrhea.—In addition to these four severely ill infants, eight additional infants were observed to develop mild gastroenteritis with or without skin lesions during the 12-day period between June 17, when the first infant developed symptoms, and June 29, the day that the last infant developed diarrhea. The clinical manifestations in these infants and the results of the bacteriological studies performed on them are also summarized in Table 1. It may be seen that two infants in the group had a moderate degree of diarrhea and pustular skin lesions of sufficient severity to require treatment (Patients 1 and 9). Coagulase-positive staphylococci were isolated from both of these infants. These two infants appear, in retrospect, to represent the first cases in the outbreak, since no evidence of skin infection or diarrhea had occurred in the nursery for at least two months prior to this time.

The other six affected infants had mild diarrhea. From four or five to many green watery stools were passed over a period of 24-48 hours. No generalized symptoms, skin lesions, or tetany were observed in any of these babies. Each of the infants recovered uneventfully. Treatment of Patients 1 and 9 consisted of administration of oral erythromycin, 50 mg/kg/day for three days. Oral neomycin, 50 mg/kg/day for four days was given simultaneously beginning on the night of June 27 to each infant remaining in the nursery.

Bacteriological Studies.—Results of bacteriological studies performed on the 12 infants are summarized in Table 1. A coagulase-positive, hemolytic, Staphylococcus aureus was isolated from the nose, skin, umbilicus, and feces of the three surviving severely affected infants. Blood cultures of all four babies in this group were sterile. The cultures of feces inoculated on blood agar plates were perhaps the most revealing. Feces cultured in this way grew out almost pure cultures of staphylococci in six of eight infants so examined. Gram-stained smears of the same fecal specimen in five of the six culturally positive specimens showed Gram-positive cocci as the

overwhelmingly predominent micro-organism. Cultures of these same specimens on selective media for Salmonella or Shigella and serological examination of the isolated Escherichia coli for pathogenic serotypes were negative. Fecal cultures failed to give evidence of staphylococcal infection, therefore, in two of eight affected infants, as well as in the three unaffected infants (Patients 11, 13, and 17) who were cultured.

In vitro sensitivity to various antibiotics of the staphylococci isolated from three of the infants is given in Table 2. These data, obtained by the tube-dilution technique, show that the micro-organism isolated from each infant had a nearly identical spectrum of sensitivity to the antibiotics tested. The antibiotic sensitivity spectrum of the Staphylococcus isolated from these infants was characteristic of the "hospital" strains for the period of time under consideration.[23]

Epidermiological Observations. — With recognition of the extent of the outbreak, the newborn nursery was closed to further admissions on June 25, 1954, and the severely ill infants were transferred to an isolation ward.

The relationships between date of birth and development of symptoms are summarized in Figure 4 for each infant in chronological sequence according to birth date. The duration of stay in the nursery is given by the total length of the bar, the onset and duration of symptoms by the clear or cross hatched area. From this diagram it may be seen that two infants (Patients 1 and 5) had developed symptoms five and two days, respectively, prior to onset of illness in Patient 10. An additional infant (Patient 9) developed diarrhea and skin lesions the same day and was discharged improved but still on therapy. A 36- to 48-hour interval separated onset in

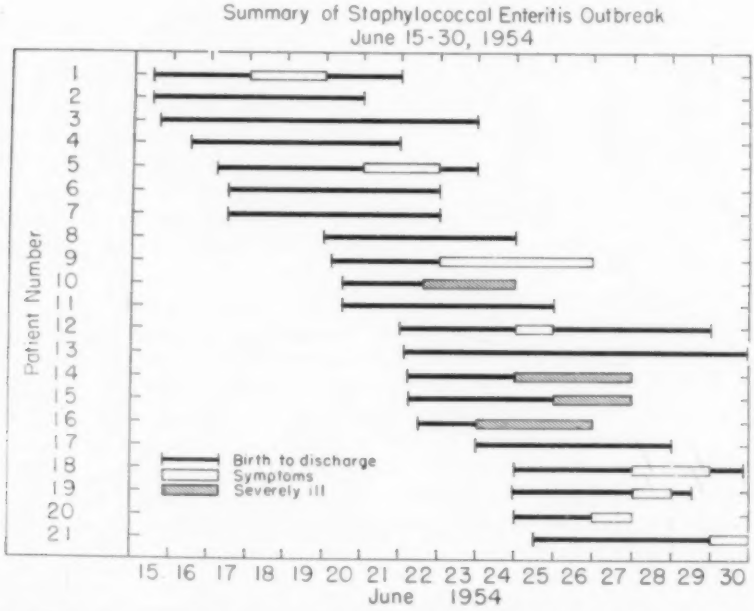

Fig. 4.—Graphic representation of the relation between the date of birth, duration of stay in nursery, and onset and duration of symptoms in each infant admitted to the nursery between June 15, 1954, and June 30, 1954. Symptoms represented include vomiting, diarrhea, or skin lesions. Cross hatched bars represent the four severely ill infants described in detail in the text. The nursery was closed on June 25, 1954, and oral neomycin was administered to each infant remaining in the nursery starting on June 27, 1954.

Patient 10 and in the three other severely ill infants (cross-hatched bars). From June 25 through June 27, four of the seven infants remaining in the quarantined nursery developed mild diarrhea.

During the 10-day period prior to closure of the nursery, therefore, a total of 12 out of 21 infants presumably exposed developed clinical illness, an attack rate of roughly 60%. However, the incubation period in this outbreak cannot be accurately determined, since the time of exposure is unknown. The period of time from birth to onset of symptoms in each patient was between two and four days, being three days in six of the infants.

From the data showing similar antibiotic sensitivity spectra for each of the microorganisms isolated from the severely ill infants, it was thought probable that all of the infants were infected by the same strain of Staphylococcus. Bacteriophage typing was therefore performed on the staphylococci isolated from these three infants as well as those obtained from the less severely affected ones. All strains isolated were nontypable with available phage.* Although the data are compatible with the assumption that all infants were affected by a single strain, there is no conclusive evidence that this is true.

If it is assumed that the infants were infected by the same strain, it may be inferred that, since the cases occurred over a 15-day period, a single massive exposure to a source of staphylococci probably did not occur. Rather, the consistency of the interval between birth and onset of symptoms suggests that the infants were exposed to a single source at, or within, a few hours after birth.

An intensive search for the source of infection was conducted. Cultures of the nasopharynx and feces were made of all personnel contacting the infants in the nursery or in the delivery rooms during the 15-day period of the outbreak. Nasopharyngeal cultures taken from a high percentage of professional and practical nursing personnel on duty in the delivery rooms and nursery during the period contained coagulase-positive staphylococci. However, since these strains, too, were nontypable with available phage, no conclusions are possible as to a source of infection.* None of the personnel was found to have open wounds, draining sinuses, or other conditions suggesting staphylococcal infection. Milk and the various utensils employed in care of the infants were also examined bacteriologically, with negative results.

* The phage typing was performed by Dr. Robert M. Wise, Department of Medicine, University of Minnesota. Available phage types included all recognized strains at the time of testing (Winter, 1954-1955).

Comment

The outstanding clinical characteristic of this outbreak of neonatal staphylococcal infection was severe gastroenteritis manifested in some of the infants. Four infants began their illness abruptly with severe retching and vomiting, with onset of diarrhea in each instance occurring later. Each infant was found to have diminished or absent peristaltic sounds, lack of abdominal distention, and absence of normal intestinal gas patterns in roentgenograms of the abdomen.

No entirely adequate explanation for the observed absence of normal intestinal gas patterning is known. It seems reasonable that depletion of gas from the intestinal tract in these infants may have resulted from the combined effects of an exaggerated expulsive factor—severe vomiting and diarrhea—and severe prostration, reducing abruptly the amount of air swallowed, as compared with that in a normal newborn infant. Recently it has been also suggested [24] that dehydration may play some role in the phenomenon of the gasless abdomen. The similarity of the roentgenographic findings in these infants and those of partial congenital upper gastrointestinal obstruction is striking and suggests that the differential diagnosis of vomiting in the newborn period associated with absence of

normal gas patterning should include early staphylococcal gastroenteritis. Diagnostic points which would assist in suspecting this condition early include the coexistence of skin lesions, diarrhea, or the presence of a predominance of gram-positive cocci in smears of gastric contents or feces.

Another unusual feature of illness in three infants was severe and persistent manifestations resembling tetany, which lasted 5 to 10 days. The condition was characterized by intermittent tonic contractions of all muscles, particularly the extensor groups, and general hyperirritability to external stimuli. At times hyperirritability was so marked and the tonic spasms were so severe as to suggest the possibility of neonatal tetanus to the observer. The serum calcium level was normal in one infant and reduced in the other infant in whom this value was determined. Lack of response to intravenously administered calcium gluconate was characteristic of two of the infants; the third, a 1800 gm. premature infant, had an elevated serum phosphorus level and responded slightly to oral calcium lactate. Appearance of this syndrome soon after starting treatment suggests a similarity to the type of postacidotic tetany described by Rapoport and co-workers,[25] in which tetany is thought to result from decreased ionized blood calcium in the presence of mild alkalosis. However, persistence of the symptoms for periods up to 10 days far exceeds the duration of disease reported by these authors. It seems possible that a more direct, as yet undefined, action of a product of the Staphylococcus on the central nervous system may have produced this effect.

Clinical features of this outbreak resemble in some ways those of staphylococcal food poisoning. Abrupt onset of severe retching and vomiting shortly followed by diarrhea, with prostration, is known to follow ingestion of foods in which certain strains of staphylococci have been allowed to establish growth. Although still in dispute,[26] it is thought by some investigators[27] that the responsible strains of staphylococci elaborate a heat-stable enterotoxin distinctive from its other well-known exotoxins.

Bacteriological evidence for the staphylococal etiology of the observed clinical syndrome is based upon isolation of this micro-organism from the nasopharynx, umbilicus, skin bullae, and feces of the affected infants. All blood cultures taken remained sterile. Of considerable practical significance was the finding that cultures of the stool of the affected infants on the usual selective media failed to reveal the presence of staphylococcal infection. Only when samples of feces were streaked on blood agar plates and examined on Gram-stained smears was it possible to determine that the Staphylococcus was the overwhelmingly predominent microflora of the intestine.

These bacteriological studies appear to give strong support to the hypothesis that the gastrointestinal tract, as well as the skin of the affected infants, was a site of a primary infection by the Staphylococcus. Such an interpretation also has support in the data from previously studied outbreaks.† The possibility cannot be excluded, however, that this epidemic may have been due to gastroenteritis of presumed viral etiology with secondary infection by the staphylococcus. Overgrowth of staphylococci in the gastrointestinal tract after alteration of the microflora such as has been reported after antibiotic therapy could conceivably result in the observed syndrome. Failure to isolate staphylococci from the feces of two of the affected group of infants might be taken as favoring this possibility. It seems equally likely, however, that the symptoms of these two infants could have resulted from the effects of enterotoxin elaborated by numbers of staphylococci too small to be detected by the bacteriologic methods employed.

In view of these considerations, the evidence for the primary staphylococcal etiology of this outbreak must remain presumptive. On the other hand, the role

† References 8 and 18; A. A. Anderson and T. A. Good, personal communications to the author.

of this micro-organism in producing the principal manifestations of disease in the severely ill infants appears well established. Moreover, this experience clearly emphasizes the dangerous potentialities of apparently isolated cases of skin infection with gastrointestinal symptoms appearing in a newborn nursery. Had more significance been accorded the first two cases of this outbreak, it might have been possible to make an earlier and correct diagnosis in the infant subjected to surgery and to have prevented infection in the other infants.

Summary

Clinical and epidemiological features of an epidemic of gastroenteritis, apparently due to coagulase-positive staphylococci, which involved 12 of 21 infants in a newborn nursery have been described. Severe vomiting followed by diarrhea, development of rapidly spreading skin lesions and epidermolysis, and an unusually severe form of tetany marked the clinical course of the four severely ill infants. Absence of the normal intestinal gas pattern in the infant whose illness signalled the beginning of the outbreak was so striking that the possibility of congenital upper intestinal obstruction was seriously entertained. Eight other infants developed mild diarrhea, and two showed skin lesions. Primary staphylococcal etiology of the outbreak of gastritis was strongly suggested by culture and demonstration of this micro-organism on Gram-stained smear from stool specimens as well as isolation from cultures of the involved skin and nasopahrynx. The attack rate in this epidemic was approximately 60%, the incubation period probably two to four days. Although no definite source of the outbreak could be identified, circumstantial evidence pointed to exposure during the first few hours of life.

The importance of early recognition of staphylococcal infection in a newborn nursery as a means of forestalling outbreaks of epidemic proportion and properly directing treatment of involved infants is strongly reemphasized by this experience.

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Case Reports

TORSION AND INFARCTION OF THE NORMAL OVARY

A Cause of the "Acute Abdomen"

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WHILE acute abdominal symptoms are not infrequently due to torsion of an ovarian cyst, such symptoms from spontaneous torsion of the pedicle of a normal ovary are rare. Downer and Brines,[3] in 1931, collected 18 cases from the literature which they considered to be true examples of torsion of the normal ovary. They included only children and young unmarried girls, in order to exclude the possibility of inflammatory disease of the adnexa as a possible predisposing cause of torsion. Their patients ranged in age from 4 months to 16 years. In addition, they reported a case of their own in a 7-year-old girl. Baron [1] also reported an instance of torsion of a normal ovary in a 7-year-old girl, and, later, torsion and infarction in the remaining ovary of the same child.[2] Another example occurring in a 7-year-old child was briefly reported by Smith [4] in 1950. We have been unable to find any subsequent references to this problem in the English literature.

Although torsion and infarction of a normal ovary is rarely included in the differential diagnosis of the acute surgical abdomen, it should be considered in young girls in view of its relatively greater frequency in this age group. In most of the recorded cases the right ovary has been involved, and a clinical picture simulating acute appendicitis has resulted. However, when the left ovarian pedicle is twisted the clinical picture may be very confusing, particularly in young girls, in whom the common forms of tubo-ovarian diseases are rare.

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From the Department of Surgery of the College of Medical Evangelists, White Memorial Hospital.

Report of Case

A 6-year-old white girl* was first admitted to the White Memorial Hospital on Nov. 4, 1954, because of left lower quadrant abdominal pain of 24 hours' duration. The pain was cramping and colicky, but without a regular cycle, and was occasionally associated with vomiting. The pain radiated into the left anterior thigh area. No significant information was obtained in the past history.

The temperature was 99 F; pulse rate, 120, and respirations, 20. The patient appeared to be in considerable distress whenever the colicky pain occurred, but she was quite comfortable between attacks. The positive physical findings were confined to the abdomen and consisted of deep, but definite, left lower quadrant tenderness. There was no rebound tenderness. One examiner noted on rectal examination a small round tender mass in the pelvis just to the left of the midline.

The urinalysis was normal. A roentgenogram of the abdomen was also normal. Red cell, white cell, and differential counts were all within normal limits.

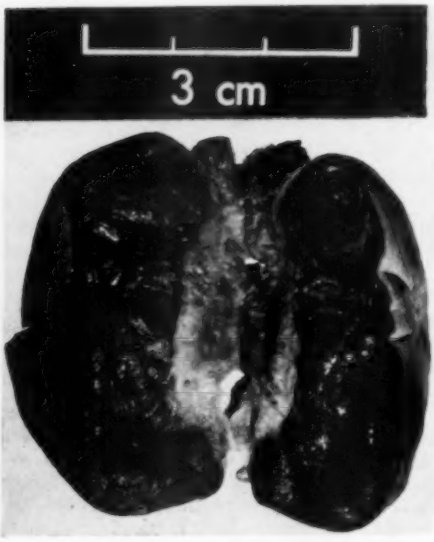
The attacks of colicky pain gradually subsided during a three-day period of observation in the hospital. The patient was then sent home with a diagnosis of abdominal pain, etiology undetermined.

The patient was readmitted 24 hours after her previous discharge because of a recurrence of the abdominal pain. The findings were identical to those of the first admission, with left lower quadrant tenderness but without rigidity or rebound tenderness. Rectal examination again revealed a small tender globular mass just to the left of the midline in the pelvis. A roentgenogram of the abdomen showed a shadow in the pelvis suggestive of an isolated dilated loop of small intestine. A complete blood cell count and urinalysis were again normal.

At exploratory laparotomy, performed Nov. 9, 1954, the left ovary was found to be swollen and hemorrhagic, measuring about 5×3 cm. A torsion of one and a half turns of the left ovarian pedicle

*Referral of Hertha Ehlers, M.D.

was present. The ovary and the twisted left ovarian tube were resected, and the postoperative course was uneventful. The pathologic examination showed infarction in an apparently normal ovary, with extensive hemorrhage in the ovarian tissue (Figure).



Infarcted left ovary from 7-year-old girl.

Comment

The etiology of torsion of a normal ovary is unknown, although it has been suggested that it may be related to an unusually long and mobile broad ligament pedicle. However, Baron's case,[2] in which there was a subsequent torsion of the opposite ovary, does not support this view, inasmuch as this ovary was noted to have a normal-appearing pedicle at the time of the patient's first operation. The adnexal torsion may consist of one or more complete twists. The intermittent and recurrent character of the acute abdominal episodes may be due to twisting and untwisting of the pedicle in the early stages of the process. Torsion of the ovarian pedicle produces circulatory stasis which is initially venous in nature but which becomes arterial as the torsion process progresses. Unrelieved torsion is likely to be followed by hemorrhagic infarction by adding arterial occlusion to early venous engorgement.

Reported cases of torsion of the ovary follow a similar clinical pattern characterized by intermittent colicky left or right low abdominal pain often accompanied by vomiting. A history of previous similar attacks is common. The physical findings are limited to deep abdominal tenderness in either lower quadrant, usually without rebound tenderness or rigidity. Radiation of pain to the genitalia or thigh may occur. In several instances a small tender pelvic mass has been noted on rectal or pelvic examination. If torsion occurs on the left side, the clinical picture may be very confusing and operation may be delayed, as it was in our reported case. A right-sided torsion is likely to be mistaken for acute appendicitis, and surgical intervention is apt to be prompt. This syndrome may also simulate acute small bowel obstruction and ureteral colic.

Immediate laparotomy with resection of the infarcted ovary and Fallopian tube would seem to be the preferred procedure. An attempt should be made to preserve some ovarian tissue in any instance in which the torsion involves the only remaining ovary. Under such circumstances an oophoropexy should be considered if, after surgical detorsion, the appearance of the ovary improves. It is possible that if the pathologic process is discovered at the venous engorgement stage the ovary might be saved.

Summary and Conclusion

Torsion and infarction of a normal ovary, although rare, can be a cause of acute abdominal symptoms, especially in young girls.

This clinical syndrome is characterized by intermittent colicky left or right lower quadrant abdominal pain often accompanied by vomiting. A history of previous attacks is common. The physical findings consist of deep localized abdominal tenderness and often a small tender pelvic mass on rectal examination.

Prompt surgical intervention is indicated, and oophorectomy is usually necessary.

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PSEUDOCYSTS OF THE PANCREAS IN CHILDHOOD

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Post-traumatic cysts of the pancreas are not uncommon in adults but are an extremely rare finding in children. Only four authenticated cases were found in the pediatric literature prior to July, 1955.* This report is of interest not only because the condition described is unusual but more on account of the importance of discovering its presence early in the course of treatment following a violent injury to the pancreatic area. The case presented below emphasizes that a pseudocyst of the pancreas in a child is potentially curable if it is excised before its damaging effects become irreversible.

Report of a Case

A 9-year-old white boy was in good health until March 25, 1955, when he was struck by a truck while he was riding on his bicycle. On admission to the Rahway Memorial Hospital soon after the accident, the child was found to be in mild shock and he complained of pain in the left upper abdominal quadrant and the periumbilical region. Palpation of the abdomen elicited generalized tenderness. The color of the skin was ashen gray. Blood pressure was 110/70 mm. Hg. A traumatic deformity of the left thigh was noted.

A roentgenogram of the left thigh showed a transverse, comminuted fracture of the middle third of the femur. On a plain film of the abdomen there was diffuse radiolucency of the left upper quadrant with moderate dilatation of the stomach, strongly suggestive of a ruptured spleen.

The patient was prepared for surgical operation by the intravenous administration of fluids and blood. On laparotomy the spleen was found to be ruptured and was excised. The pulse and respiratory rates were elevated for several days before gradually returning to normal. The body temperature fluctuated between 100 and 101 F for two weeks. A Buck's extension was applied to the left leg for treatment of the fractured femur. There was marked general improvement in the next two weeks on supportive treatment with intravenous fluids and antibiotics.

X-ray examination of the fractured femur 17 days after the accident showed overriding and lateral displacement of the proximal fragment. An open reduction was then performed and the fragments were fixed in place by a four-hole plate and screws. A hip spica was applied up to the lower costal margin. On the following day, a roentgenogram revealed good alignment and apposition of the osseous fragments.

At this time, the temperature began to spike daily to 102 and 103 F. Examination disclosed moderate nasopharyngitis which responded well to tetracycline (Achromycin). The child was discharged to home care on April 13, 1955, after six days of normal temperature.

One disturbing factor during the hospitalization was the elevation of the white blood cell count from 7500/cu. mm. on the day of admission, to 40,000, with a shift to the left in the differential count following the splenectomy. The count ranged between 30,000 and 40,000 for two weeks, then dropped to 21,000, and finally reached 10,600 four days later. At discharge, the white blood cell count was 6600/cu. mm. with a normal differential.

Second Hospitalization.—On June 17, 1955, the patient was readmitted to the hospital because of repeated emeses and marked weight loss. He had done well except for occasional vomiting until one week prior to the readmission, when the vomiting became so frequent as to produce emaciation. The hip spica was still in place but was removed after x-ray showed healing of the femur fracture with good callus formation. Now satisfactory examination of the abdomen could be done, and it showed the presence of a large, soft mass in the left upper quadrant, extending from the costovertebral angle to the umbilicus. On a plain film of the abdomen, gas-filled bowel could be seen on the right side but not on the left. Intravenous urography showed normal function of both kidneys and a suggestion of extrinsic pressure on the left kidney. After the ingestion of barium, the stomach was seen to be displaced upward and laterally by an extrinsic mass.

Differential diagnoses at this time included the following: 1. subphrenic abscess, 2. organized clot, 3. renal hygroma, 4. post-traumatic omental

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* References 1-4.

cyst, and 5. post-traumatic pancreatic cyst.

The child was given a fat-free diet supplemented by a vitamin-mineral mixture (Lactofort) and was treated conservatively until his condition permitted an exploratory laparotomy. This was performed on the 13th hospital day through a left transverse subcostal incision and exposed a large mass posterior to the gastrocolic omentum. After a small amount of clear, straw-colored fluid was aspirated from the mass, a trochar and cannula were inserted and 3500 cc. were evacuated. The collapsed cyst was then easily removed by freeing it from the stomach above and the transverse colon below and tracing it to its origin in the tail of the pancreas. The rent in the gastrocolic omentum was repaired and the abdominal wound was closed after inserting a rubber drain down to the tail of the pancreas.

The postoperative course was stormy for several days. Homeostasis was maintained by intravenous fluids, repeated transfusions, and antibiotics administered intramuscularly. The temperature became normal on the fourth day, and nourishment began to be taken by mouth. Convalesence was uneventful until the patient was discharged 13 days later. A final follow-up examination in three months revealed a completely normal youngster who was gaining weight rapidly and had returned to full activity.

Pathological Report.—Gross examination revealed a large cyst wall measuring 22 cm. when flattened out. The wall was thickened and fibrous, and showed a smooth endothelial lining without evidence of malignancy. On microscopic examination, the cyst wall was lined with widely separated flattened, undifferentiated cells. The underlying wall was made up of edematous collagenous, fibrous tissue showing numerous vascular channels and foci of inflammatory infiltration. There was no epithelial lining. The diagnosis was pseudocyst of the pancreas.

Comment

Mithoefer[1] reviews pancreatic cysts in childhood and presents the following classification:

1. *Pseudocysts.*—Have no true epithelial lining and are composed of granulation tissue in varying stages of development, surrounding the more or less liquid products of pancreatic destruction and fat necrosis.
2. *Retention Cysts.*—Results from partial obstruction of a major pancreatic duct and have a lining of duct epithelium; usually follow chronic pancreatitis.
3. *Neoplastic Cysts.*—Are rare and are usually one of three types: (*a*) benign cystadenoma, (*b*) cystadenocarcinoma, (*c*) dermoid or teratoma.
4. *Congenital Cysts.*—Have neither neoplastic nor retention factors and are usually associated with polycystic disease elsewhere.
5. *Parasitic Cysts.*—Are mostly due to Echinococcus infestation and are rarely encountered in this country.
6. *Fibrocystic Disease.*—Is not usually characterized by gross cyst formation.

This case appears to be one of pseudocyst and therefore falls in the first group. The clinical picture and the pathological findings are characteristic. The pathogenesis usually includes abdominal trauma, biliary-tract disease, or pancreatitis preceding the development of an upper abdominal mass. The trauma from the automobile accident, which was violent enough to produce a ruptured spleen and a comminuted fracture of the femur, could have easily injured the pancreas. As a result enzymes were released into the lesser omental bursa with the development of chemical inflammation, fat necrosis, and tissue autolysis. Granulation tissue and the surrounding viscera could then encapsulate the liquefied mass and form the cyst which would remain asymptomatic until it became large enough to cause obstruction or abdominal distension.

In retrospect, the two-week period of fever and leucocytosis following splenectomy must have been the period of traumatic pancreatitis which initiated the cyst formation. Earlier recognition of the presence of the cyst was hampered by inability to palpate the abdomen with the body cast in place. The presence of a cyst could be suspected only when it became large enough to compress and displace the stomach with ensuing vomiting and marked weight loss. Fortunately, the removal of the cyst was accomplished early enough to relieve all of the distress symptoms and eventuate in complete recovery and restoration of normal nutrition.

Summary

This is one of the few recorded cases of a pseudocyst of the pancreas found in a child. The probable pathogenesis following trauma is discussed. The diagnosis was based on the location of the injury and the development of a mass in the region of the pancreas. Excision of the cyst confirmed the diagnosis and resulted in the complete recovery of the patient.

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DISCORDANCE OF CRETINISM IN MONOZYGOTIC TWINS

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SPORADIC (nongoitrous) cretinism occurring in one of monozygotic twins strongly suggests the etiology of that condition to be not genetically conditioned but, rather, related to direct influences of environmental factors on the development of the thyroid anlage in the fetus. This is to be differentiated from goitrous sporadic cretinism, which is thought to be genetically conditioned.[1] The near absence of familial coincidence of nongoitrous sporadic cretinism lends further support to that hypothesis. To date, three proved instances, and one probable, of discordant cretinism in monozygotic twins are reported.*

In contrast, where congenital disorders are considered genetically conditioned, it is common to observe manifest disease in each of identical twins; for example, in known instances where vitamin-D-resistant rickets has occurred in one monozygotic twin, it has also been present in the other.†

This communication records a fourth proved instance of discordance between identical twins, one of whom manifested congenital cretinism.

Report of Case

Twin girls, one of whom was a cretin, were born of Mexican parents on Dec. 21, 1950, following an uncomplicated pregnancy and easy delivery. At the time of the twins' birth, the father and mother, 26 and 24 years of age, respectively, were both in good health. This was the mother's first pregnancy, during which she received supplemental calcium and vitamins. The diagnosis of twinning was made two weeks prior to delivery.

This child was the first-born twin and weighed 2130 gm. At delivery there was one placenta, and the parents were told that the babies were identical twins. The baby appeared normal at birth and was indistinguishable from her sibling. She was kept in an incubator two weeks and then discharged home with her sister. By 3 weeks of age it was noted that she was "different" from her twin. Her tongue had become large, her skin was "blue and cold," her eyes seemed to slant, and she was fat. An umbilical hernia developed, her cry became hoarse, she developed difficulty with swallowing, and constipation became prominent (Fig. 1).

Fig. 1.—Cretin (left) and twin at 6 weeks of age.

At 6 weeks of age, the local physician made the diagnosis of hypothyroidism, and thyroid therapy (dosage unknown) was instituted and continued to age 2 years. The major signs and symptoms of the disorder quickly vanished with treatment. She stood at about 9 months of age, walked at 1 year, talked at about 18 months, and at the age of 2 years she was almost the same height as her twin and was "as bright and as alert." When she was 2½ years old, therapy was discontinued, and she remained untreated for the next two years. Signs of hypothyroidism quickly reappeared after cessa-

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Present address of Dr. Pickering, University of Oregon Medical School, Portland, Ore.

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tion of treatment. Her facial expression became dull, her tongue became large, her appetite decreased, and growth slowed. Her skin and hair became dry and coarse. She became constipated and somnolent.

She was admitted to this hospital for study at the age of 4 years 3 months, at which time she appeared classically cretin and resembled her twin only vaguely (Fig. 2). She was short and stocky,

Fig. 2.—Twins at 4 years 3 months. The cretin had been off thyroid therapy for two years.

with dull, puffy facies, open mouth and protruding tongue. Her skin was pale with a yellowish tinge, dry and very coarse, and with moderate hypertrichosis present. Her hair was thick and dry. The thyroid gland was not palpable. The abdomen appeared protuberant, and the liver edge was palpable 1 fingerbreadth below the right costal margin. The remainder of the physical examination was not remarkable. Essential growth and laboratory data are shown in Table 1.

Blood studies, to validate the identical nature of the twins, are shown in Table 2.

Therapy with sodium *l*-thyroxine, 0.1 mg. daily, was instituted and continued for two weeks, when it was increased to 0.15 mg. per day. She remained on that dose for nine months. After two weeks of therapy, she had lost 1.8 kg. and became more active. After three months of treatment, all outward signs of thyroid deficiency had disappeared. Her physical appearance, as compared to that of her twin, after nine months on sodium *l*-thyroxine, is shown in Figure 3.

Fig. 3.—Twins at 5 years. The cretin had been on sodium *l*-thyroxine therapy for nine months.

The normal twin was the second born and weighed 1830 gm. Her growth and development were entirely normal. She stood at 9 months, walked at 12 months, and talked at 18 months. She was admitted to the hospital along with her twin for study and was followed in the outpatient clinic for the nine months preceding this study for comparison with her sibling. Her development has continued to be normal (Table).

Comment and Summary

The common placenta and identical blood pedigree validates the twins' monozygotic origin.[7] Cretinism in one twin is documented by the history of classical signs and symptoms and appearance (Fig. 1) in early infancy and by her appearance and laboratory studies in this clinic (Fig. 2 and Table).

Sodium-*l*-thryoxine in adequate dosage effected a prompt and continuing change

TABLE 1.—*Growth and Laboratory Data*

Patient	Age, Yr.-Mo.	Ht., Cm.	Wt., Kg.	I. Q.	Bone Age, Yr.-Mo.	B.E.I. x/100 Cc.*	I^{131} Uptake†	Thyroxine Therapy, Mg. Daily
Cretin	4-3	84.25	12.9	80	1-3	0	Before T.S.H. 4.6%; after T.S.H. 3.1%‡	0.15
	4-6	89.50	12.3			11		
	4-9	91.75	12.2	80	1-9			
	5	94.50	14.6		2-6			
Normal twin	4-3	96.5	12.8	90	2-6	5	Before T.S.H. 22.4%; after T.S.H. 41.6%	None
	4-6	97.9	14.6					
	4-9	99	15	91	3			
	5	101	15		4			

* B.E.I. indicates butanol-extractable iodine.
† I^{131} uptake studies preceeding and following administration of T.S.H. were done according to the technique of Pickering, D.E., and Miller, E.L.: A. M. A. Am. J. Dis. Child. 85: 135-140 (Feb.) 1953.
‡ T.S.H. indicates thyroid-stimulating hormone.

toward a normal metabolism and physiognomy (Table and Fig. 3), in accordance with its previously established value‡ in the therapy of hypothyroidism in infancy and childhood.

In summary, this fourth known instance of proved discordance of sporadic cretinism in monozygotic twins lends credence to the assumption that this disorder is not genetically determined, but rather is secondary to as yet unknown environmental factors in utero.

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TABLE 2.—*Blood Pedigree*

	Type	Rho (D)	RH′ (C)	Rh″ (E)	Hr′ (c)	Hr″ (e)	Cw	Kell	Fya
Father	A_1 MM	+	+	−	−	+	−	−	+
Mother	A_1 NN	+	−	−	+	+	−	−	−
Cretin	A_1 MN	+	+	−	+	+	−	−	+
Normal	A_1 MN	+	+	−	+	+	−	−	+

Progress in Pediatrics

Pulmonary Coccidioidomycosis in a Twenty-One-Day-Old Infant

Report of a Case and Review of the Literature

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Introduction

Coccidioidomycosis, first described by Posadas in 1892, has become sufficiently well known by now to render a description of the disease as part of this review unnecessary. Classical descriptions can be found in articles by Posadas,[1] Wernicke,[2] and Rixford and Gilchrist.[3] Important advances were made by Ophüls * and Dickson.†

The more thorough recent articles include the study of the pathology of the disease, with a chronological survey, by Forbus and Bestebreurtje,[8] the thorough literature review by Schwartz and Muth,[9] and two of many articles by Smith.‡

However, there has been no published analysis of reported pediatric cases of coccidioidomycosis. In an attempt to prepare one, the literature was searched for all articles that might contain case reports. A total of 242 articles were reviewed, containing reports on 561 cases. Of these 561 cases, 99 were in the age group up to 16 years.

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* References 4 and 5.

† References 6 and 7.

‡ References 10 and 11.

Analysis

1. *Age* (Table 1).—Of the 99 pediatric patients, there was 1 under 1 month of age, 13 between 1 month and 1 year, 38 between 13 months and 6 years, and 46 between 7 and 16 years of age. In one case, the child's age was not stated.

TABLE 1.—*Cases by Age Groups*

Cases, No.					
0-1 Mo.	1 Mo.-1 Yr.	13 Mo.-6 Yr.	7 Yr.-16 Yr.	Age Unknown	Total
1	13	38	46	1	99

2. *Locality* (Table 2).—As would be expected from the known distribution of the disease, the great majority of cases (83) were reported from California. Arizona with 8 cases and Texas with 6 contributed to a total of 97 cases from endemic areas. The one case reported from Kansas can be traced to exposure in Texas. The case reported from China is somewhat doubtful.

TABLE 2.—*Locality Where Reported*

	Cases, No.					
	0-1 Mo.	1 Mo.-1 Yr.	1-6 Yr.	7-16 Yr.	Age Unknown	Total
Arizona	0	0	2	6	0	8
California	1	11	32	38	1	83
Kansas	0	0	1	0	0	1
Texas	0	1	3	2	0	6
China	0	1	0	0	0	1
Total	1	13	38	46	1	99

The geographical distribution in the various age groups does not vary from this picture.

3. *Race or Nationality* (Table 3).—This is unknown in 9 of the 99 cases. Of the remaining 90 patients, 37 are white, 22 of

TABLE 3.—*Race or Nationality*

	Cases, No.					
	0–1 Mo.	1 Mo.–1 Yr.	1–6 Yr.	7–16 Yr.	Age Unknown	Total
White	1	5	13	18	0	37
Mexican	0	4	11	7	0	22
Negro	0	2	10	16	1	29
Oriental	0	1	0	1	0	2
Unknown	0	1	4	4	0	9
						99

Mexican origin, 29 Negro, and 2 Oriental. Even considering the relatively high percentage of Mexicans in California, the number of cases among Mexicans and Negroes is disproportionately high. This could reflect either higher racial susceptibility or greater exposure to dust, the parents often being migrant laborers, etc., or both.

The distribution in the various age groups is similar, except for few Negroes (2 out of 12) in the one-month to one-year group. With the small size of this group, this is not necessarily significant.

4. *Sex* (Table 4).—The sex of the patient is not stated in five cases. Of the others, 57 are boys and 37 girls. In infants,

TABLE 4.—*Sex*

	Cases, No.					
	0–1 Mo.	1 Mo.–1 Yr.	1–6 Yr.	7–16 Yr.	Age Unknown	Total
Male	0	7	24	26	0	57
Female	1	5	11	19	1	37
Not stated	0	1	3	1	0	5
						99

the distribution between the sexes is almost equal, but in the preschool group of 1- to 6-year-olds there are 24 boys to 11 girls. This probably reflects the greater tendency of boys of this age to play outdoors.

In the 7- to 16-year group, there are 26 boys to 19 girls, a fact which might also indicate increased exposure of the boys.

5. *Presenting Complaint.*—These can be classified into various groups. These referable to the respiratory system include dyspnea, cough, chest pain, etc.; these referable to the skeleton and soft tissues, swellings, ulcers, joint pains, abscesses, skin lesions, etc.

In the 99 cases, the presenting complaint was referable to the skeleton or soft tissues in 37, to the respiratory system in 23, to both in 6, to the central nervous system in 9, to other systems in 6, and not listed in 18 cases.

In the 1-month to 1-year and 1- to 6-year groups, complaints were more frequently referable to the skeleton and soft tissues than to the respiratory system (6 to 2 and 19 to 6 cases). In the older, 7- to 16-year group the respiratory complaints predominated, 15 to 11.

6. *Location of Main Lesion.*—This was found in the lungs in 40 cases, in bone in 38, in the skin or soft tissues in 10, in the central nervous system in 4, widely disseminated in 5, and in the eye in 1 case. The location was not stated in one case. In many of these cases, evidence of early primary lung involvement might have been inconclusive by the time other lesions were found.

Bone lesions predominate over pulmonary lesions 8 to 1 and 16 to 14 in the infant and preschool groups, with pulmonary lesions dominating 25 to 14 in the oldest group. Many cases of residual cavities are reported in this group.

Clinical Picture.—Of the 97 cases in which this is stated, the clinical picture of the disease is distributed as follows: Osteomyelitis, 37 cases; residual pulmonary cavity, 13 cases; "valley fever," 11 cases; pneumonia, 5 cases; primary tuberculosis, 5 cases; meningitis, 5 cases. Three cases each: ulcerating skin granuloma, subcutaneous abscess. Two cases each: bronchopneumonia, diffuse pulmonary infiltration, pleurisy, malignancy. One case each: miliary pulmonary infiltration, draining sinuses, Hand-Schüller-Christian disease, encephalitis, endophthalmitis, bronchitis, and undetermined upper respiratory infection.

8. *Diagnostic Methods Used.*—In 26 cases, "direct" methods, depending on demonstration of the organism (biopsy, smear, autopsy, culture, inoculation), were used alone. In 41 cases, these methods were used together with "indirect" methods (serological studies, skin tests). The total is 67 cases.

"Indirect" methods alone were used in 27 cases. In five cases, the method used was not stated.

Specifically, coccidioidin skin tests were used in 58 cases, culture and/or animal inoculation in 46, serological studies in 42, smears in 24, biopsy or autopsy in 22.

9. *Duration of the Disease.*—This was stated in only 59 of the 99 cases. Of these, 8 lasted less than one month, 15 from one to three months, 19 from three months to one year, and 17 cases lasted over one year.

10. *Treatment.*—As is well known, no truly curative treatment is known as yet. Many methods were used in the cases studied, but none in a sufficient number of cases to allow an evaluation of their value. The treatment used was mentioned in only 39 of the 99 cases.

11. *Outcome.*—This is unkonwn in 27 cases out of 99. If in the remaining 72 cases we classify the cases by age group (Table 5), a decline in mortality with increase in age is evident. The mortality rates are 100% under 1 month of age (1 case), 45% in the 1-month to 1-year group, 27% in the 1-year to 6-year group, and 12% in the 7- to 16-year group. The average over-all mortality in the 72 cases is 33%.

TABLE 5.—*Outcome by Age Groups*

	Cases, No.					
	0-1 Mo.	1 Mo.-1 Yr.	1 Yr.-6 Yr.	7-16 Yr.	Age Unknown	otal
Recovered	0	6	19	29	0	54
Died	1	5	7	4	1	18
Unknown	0	2	12	13	0	27
Total	1	13	38	46	1	99
Mortality (excluding unknown)	100%	45%	27%	12%	100%	33%

Grouping these cases by type of clinical picture (Table 6), the mortality is highest in central nervous system involvement (100%) and in osteomyelitis (53%). (It is to be noted that the outcome is known in only 15 of 37 cases of osteomyelitis and that the knowledge of it in the other 22 could completely change the picture.) The mortality is zero in the 13 reported cases of residual pulmonary cavity and the 11 reported cases of "valley fever." Intermediate rates are seen in other types of pulmonary involvement (23%) and in skin and soft tissue involvement (14%).

TABLE 6.—*Outcome by Clinical Type*

	Cases, No.								
	Osteomyelitis	Resid. Pulmo. Cavity	"Valley Fever"	Other Pulm.	CNS	Skin & Soft Tissue	Other	Not Known	Total
Recovered	8	13	11	13	0	6	2	1	54
Died	7	0	0	4	5	1	0	1	18
Unknown	22	0	0	2	1	2	0	0	27
Total	37	13	11	19	6	9	2	2	99
Mortality (excluding unknown)	53%	0%	0%	23%	100%	14%	0%	50%	33%

The methods of treatment include bed rest, general symptomatic and supportive treatment; curettage of lesions, local excision, amputation, pneumothorax, pulmonary resection, and lobectomy; coccidioidin vaccine; penicillin, streptomycin, oxytetracycline (Terramycin); colloidal copper, thiazolsulfone (Promizole), stilbamidine, emetine, antimony potassium tartrate (tartar emetic), Actidione, formalin, hydriodic acid, mercury bichloride, Thiocymetin, ethyl vanillate, trisulfapyrimidines, aminosalicylic acid, isoniazid, and deep x-ray therapy.

By racial or national groups (Table 7), the mortality rates for the 72 cases with known outcome are 19% in whites, 30% in Mexicans, 44% in Negroes, and 0% in the 2 Orientals. The patients' race is not

TABLE 7.—*Outcome by Race or Nationality*[a]

	Cases, No.					
	White	Mexican	Negro	Oriental	Unknown	Total
Recovered	10	10	6	1	3	30
Died	6	4	4	0	4	18
Unknown	7	5	15	0	0	27
Total	23	19	25	1	7	75
Mortality (excluding unknown)	37%	28%	40%	0%	57%	37%

[a] Omitting the 0 mortality groups of residual pulmonary cavities and "valley fever."

listed in 9 cases, of which 4 were fatal. It it is to be noted that of the total of 29 Negroes, the outcome was not stated for 16; thus the mortality values in this group might be quite different from these given here.

Omitting the zero mortality groups of residual cavities and of "valley fever," the rates are 37% in whites, 28% in Mexicans (the reverse of those in the entire group), 40% in Negroes, O in the one Oriental (over-all rate 37%).

Thus, no definite conclusions can be drawn regarding racial differences in mortality, though a higher mortality in Negroes is likely.

Cases in Infants

A total of 14 cases have been reported (Table 8), the youngest being in a 3-week old infant with a picture of pneumonia, later dissemination, and death in five weeks.[12] No fatal pediatric cases with miliary pulmonary lesions alone have been reported previously.

Of the 14 cases, the outcome is not stated in 3. One infant recovered from a residual lung lesion after a primary infection; three recovered from osteomyelitis, and one recovered from a possible coccidioidal endophthalmitis.

Of the six who are known to have died, two had mainly pulmonary symptoms with later dissemination, two had osteomyelitis with dissemination, one had a cervical abscess, and the clinical picture is not stated in one case.

Report of Case

History.—A 21-day-old Mexican boy was admitted to Mercy Hospital on Oct. 7, 1955, with a complaint of progressive dyspnea, cyanosis, and nonproductive cough of about 24 hours' duration. The infant had been delivered at Mercy Hospital under general anesthesia with the application of low outlet forceps and with no complications. The infant was discharged from the newborn nursery five days later in apparently good condition.

Physical Examination.—Physical examination disclosed a well-developed well-nourished white boy appearing ill, markedly dyspneic, and slightly cyanotic. The temperature was 98 F rectally, the pulse rate 120 per minute, and the respirations 52 per minute. The head and neck were not remarkable, except for cyanotic lips. There was no

TABLE 8.—*Cases Reported in Infants*

Case Number	Year	Authors	Age, Mo.	Outcome	Clinical Type
1	1929	Cummins, Smith, & Halliday	4	Died	Unknown
2	1929	Evans & Ball	3	Died	Cervical abscess
3	1929	Jacobson	3	Died	Pulmonary, then dissem.
4	1931	Chou & Reiss	6	Recovered	Endophthalmitis
5	1932	Caldwell	7	Recovered	Osteomyelitis
6	1949	Cohen	6	Recovered	Osteomyelitis
7	1953	Dykes, Segesman, & Birsner	5	Recovered	Osteomyelitis
8	1953	Dykes, Segesman, & Birsner	6	Unknown	Unknown
9	1953	Dykes, Segesman, & Birsner	5	Unknown	Unknown
10	1953	Dykes, Segesman, & Birsner	6	Died	Osteomyelitis, then dissem.
11	1953	Dykes, Segesman, & Birsner	12	Unknown	Unknown
12	1953	Dykes, Segesman, & Birsner	12	Died	Osteomyelitis, then dissem.
13	1953	Townsend & McKey	¾	Died	Pulmonary, then dissem.
14	1954	Cotton & Others	7	Recovered	Residual cavity from pulmonary

evidence of respiratory obstruction.

The chest showed rapid symmetrical expansion and was resonant throughout on percussion. Diffusely scattered dry and subcrepitant rales were heard bilaterally through all lung fields. The heart did not appear enlarged; the rhythm was regular with tachycardia, and no murmurs were heard. The examination of the abdomen, extremities, central nervous system, and skin revealed nothing remarkable.

Laboratory Findings.—Blood count on admission: 12.6 gm. of hemoglobin per 100 ml.; 10,750 W.B.C. per cubic millimeter, with 71% neutrophiles, 25% lymphocytes, and 3% monocytes. Urinalysis on admission: normal. Chest roentgenogram on admission: patchy consolidation involving the entire lung fields bilaterally.

Blood count on the fifth hospital day: 15.8 gm. of hemoglobin, per 100 ml.; 15,050 W.B.C. per cubic millimeter, with 18% band forms, 13% segmented neutrophiles, 4% eosinophiles, 1% basophiles, 51% lymphocytes, and 13% monocytes. Chest roentgenogram on the fifth hospital day: no change from the previous roentgenogram.

The clinical diagnosis was bronchopneumonia and possible congenital heart disease.

Clinical Course.—The patient was placed in oxygen to which Alevaire was later added; antibiotics were administered, and stock formula was given. He very easily became cyanotic upon being removed from the oxygen tent, when crying or taking feedings. Some dyspnea was constantly present. Formula and oral electrolyte solutions were taken readily.

The patient was mostly afebrile with occasional low-grade fever ranging from 99 to 101 F rectally. He did not respond to different antibiotics, and there was no change in the chest findings during the first few hospital days.

On the fifth hospital day cyanosis became constant, despite an oxygen content of 55% in the tent. Upon being removed from the tent, the child's face promptly turned dark blue. Diffuse crepitant rales, rhonchi, and wheezes were heard in the lungs, but no heart murmurs were heard. There were never any findings suggestive of central nervous system involvement.

On the seventh day the child was digitalized with digitoxin. His condition deteriorated rapidly, with irregularly varying pulse and respiratory rates during the night. He developed extreme bradycardia and bradypnea and died, on the eighth hospital day.

Family History.—The family history showed that the mother had had an operation in September, 1954, for an allegedly post-traumatic draining lesion on the right foot, with good results and no further drainage. The father and three siblings were in apparent good health.

Further information was later obtained through the courtesy of Dr. Sergio de la Garza, from the Department of Pathology of the Hospital Universitario, Universidad de Nuevo Leon, Monterrey, Mexico, where the mother had been operated upon. This disclosed that the mother's lesion had been a coccidioidomycotic granuloma of the right calcaneus from which specific causative organisms were microscopically demonstrated.

The mother was born in Chicago. From age 6 to 14 she resided in Zacatecas, North Central Mexico, returning then to the United States. Subsequent questioning revealed that she had been in Southern California and in Texas for short periods of time prior to the appearance of her symptoms in 1951. At the present time her lesion is apparently well healed, clinically and roentgenologically, and her chest roentgenogram is negative.

Postmortem Examinations.—The positive gross findings were limited to the lungs. The heart and lungs were removed en bloc and weighed 214 gm. The heart was normal, except for a patent foramen ovale and a patent ductus arteriosus.

Both lungs showed extensive nodular consolidation and were covered subpleurally with multiple nodular yellow elevations of moderately firm consistency, varying from 1 to 10 mm. in diameter and with yellow nodular mottling (Fig. 1). On section, the lungs cut with distinct firmness and the surface was thickly studded with similar yellowish-white nodules, some of them appearing larger because of a confluency of the nodules (Fig. 2). Some of the largest were partly necrotic in the center and beginning to liquefy. The process was so extensive that almost two-thirds of the lung parenchyma appeared to be replaced by the granulomatous tissue. The trachea and bronchi contained thick mucus, and the mucosal surfaces appeared hyperemic. The hilar nodes were not enlarged, nor were they grossly involved by the granulomatous process.

On microscopic examination, the lungs were found to contain compact granulomata composed of loosely packed epithelioid cells with occasional giant-cell forms of the Langhans type. Occasional focal areas of necrosis were seen throughout the section. Scattered throughout were round and oval spheres surrounded by a doubly refractile limiting membrane (Figs. 3 and 4), and some containing refractile hyaline material and others containing numerous small spherical spores. Some spheres showed rupture of their capsules, with dispersion of the small spores into the surrounding interstitial tissue, with marked leucocytic infiltration and the production of microabscesses.

The peribronchial nodes contained a few microscopic granulomas containing parasites, and in the spleen there was a single granuloma, also containing a parasite. The liver showed only mild fatty infiltration. The pancreas, kidney, and adrenal

Figure 1

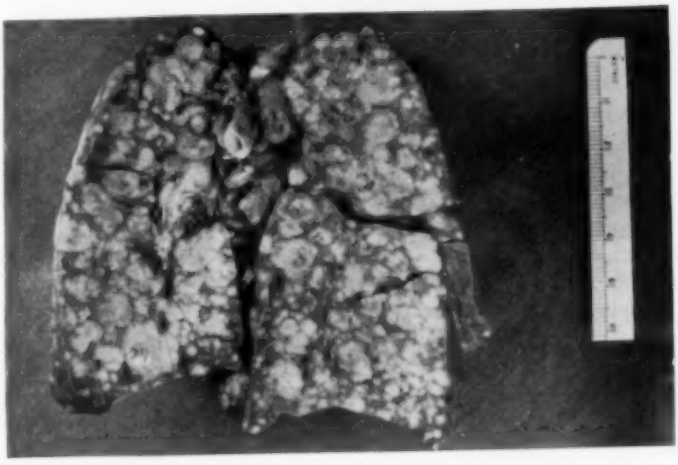

Figure 2

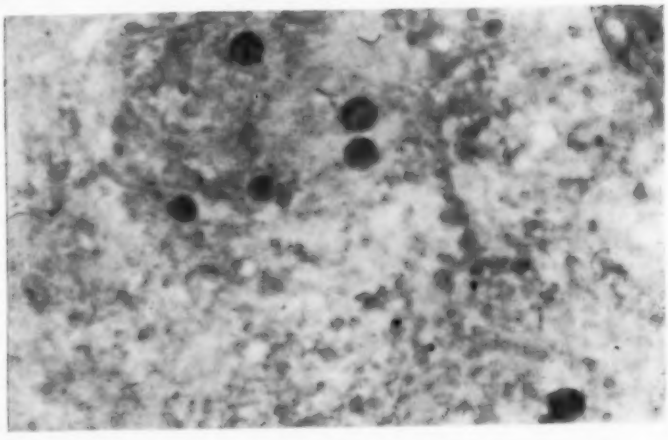

Figure 3

Figure 4

presented only congestion. Permission to study the brain could not be obtained.

The pathological diagnosis was bilateral pulmonary coccidioidomycosis, with minimal microscopic dissemination to peribronchial nodes and spleen.

Comment

The case reported here is unusual for these reasons: (1) the age of the patient (there being only one reported previous case in an infant under one month of age); (2) the apparent contraction of the disease in Chicago, far from an endemic area, and (3) the unusual pathological findings—this being the first reported fatal case in a child with miliary pulmonary and lymphatic lesions exclusively.

The question as to how the infection was acquired poses an interesting problem. The child was born in a hospital; thus, in clean conditions. Transplacental infection has been practically disproved by reports of nine cases with infected mothers and even placentae with no evidence of infection in the fetus or child. It is tempting to think of the mother as the source of infection, but her lesion was closed at the time the baby was born, and the endospores found in the body are not infective by inhalation or ingestion.

The fact that the pathological findings were limited to the lungs speaks for the respiratory route of infection, which is by far the most usual one in this disease. This presupposes the presence of infective chlamydospores, which develop outside the human body and are found in the soil and in dust in endemic regions. It would seem that the mother's lesion was the most likely source of the organism, which then had to develop to the chlamydospore stage outside the body.

Speculative though this theory is, it seems to be the least unlikely explanation.

Summary

A review and analysis of 99 reported cases of coccidioidomycosis in children is presented. Of these, 14 cases were in infants. The significant findings include the following:

1. The majority of the cases are from California.

2. A high proportion of Negroes and Mexicans is found, with no definite correlation of race and mortality.

3. The sex distribution shows definitely more cases among boys than among girls in the preschool age group.

4. Osteomyelitis is the commonest of a wide variety of reported clinical pictures.

5. Mortality average is 33%, being higher in infants and decreasing with increasing age.

A case of fatal coccidioidomycosis of eight days' duration in a 3-week old infant in Chicago is presented. The disease was diagnosed at autopsy, and the positive findings were limited to multiple nodules in the lungs. The child's mother had a healed coccidioidomycotic bone lesion. The possible source of the infection is discussed.

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Correspondence

SOB SPASM

To the Editor: The many French-speaking readers of the A. M. A. JOURNAL OF DISEASES OF CHILDREN were much interested in the paper by Alanson Hinman and Lloyd B. Dickey on "Breath-Holding Spells" and in th psychological and psycho-analytical developments of the authors (Vol. 91, N. 1).

I should however like to point out to your readers that the syndrome in question, well known since Rilliet and Barthez, mentioned in your Journal with reference to a German translation, has been known in France as *"spasme du sanglot"* (sob spasm), a name which I proposed in 1948 and which has been generally accepted. The clinical description, diagnosis, treatment, encephalography, and the difference from epilepsy, spasmophilia, tetany, etc., are taught to our young students under the name of "sob spasm". This indication may help American authors in search of information on the subject beyond the range of the literature available in English.

Below are listed some French papers on this matter:

Debré, R. et Mlle. Lévy: Le spasme du sanglot et son diagnostic, Nourrisson 20-3:73-90, 1932.

Debré, R.; Mozziconacci, P.; Masse, N. P., and Lerique-Koechlin, A.: Le spasme du sanglot: clinique et electroencéphalographie, Semaine hôp. Paris 24:1477-1480 (June 18) 1948.

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Abstracts from Current Literature

This issue marks a departure in the method of abstracting current literature. Heretofore, a loyal group of physicians have contributed abstracts from various journals on a wide range of subjects. However, the large number of journals being abstracted made it very difficult to keep publication current. Since more complete abstract services are now available, and because many readers have requested an opportunity to review the tables of contents of certain journals, the Editorial Board has changed the method of abstracting. Starting with the January, 1956, issues of a selected group of journals, that portion of the table of contents dealing with subjects of pediatric interest will be published each month. The following journals will be abstracted.

Acta pædiatrica
American Heart Journal
The American Journal of Medicine
American Journal of the Medical Sciences
American Journal of Pathology
The American Journal of Roentgenology, Radium Therapy and Nuclear Medicine
The American Review of Tuberculosis and Pulmonary Diseases
Annales paediatrici
Annals of Internal Medicine
Antibiotic Medicine
Archiv für Kinderheilkunde
Archives of Disease in Childhood
A.M.A. Archives of Internal Medicine
Blood
Boletín médico del Hospital Infantil
British Medical Journal
Bulletin of the Johns Hopkins Hospital
Canadian Medical Association Journal
Circulation
Endocrinology
Helvetica paediatricia acta
Journal of the American Medical Association
Journal of Biological Chemistry
Journal of Clinical Investigation
The Journal of Nutrition
The Journal of Pediatrics
The Journal of Tropical Pediatrics
Lancet
La presse médicale
Medical Journal of Australia
Medizinische Klinik
Metabolism
Minerva pediatrica
Monatsschrift für Kinderheilkunde
New England Journal of Medicine
Radiology
Revista española de pediatria
Rivista di clinica pediatrica
Zeitschrift für Kinderheilkunde

From these the reviewer will select one or two outstanding articles for abstracting.

Obviously all the world's pediatric journals cannot be included, but depending

on available space some others may be added later. Occasionally a given issue of a journal will not be listed if no article of pediatric interest is in that particular number. During this change-over we will also continue to publish conventional abstracts until our backlog of 1955 abstracts is printed.

Acta pædiatrica, Stockholm

45: No. 1 (Jan.) 1956

Studies in Maternal Deprivation in Infants' Homes. G. Klackenberg.—p. 1.
Blood Gas Determinations on Premature Infants: I. Investigations of Premature Infants Without Respiratory Complications. W. Blystad.—p. 13.
Paper Electrophoresis of Serum Proteins in Infantile Toxicosis. C. Choremis, and C. Moschidis.—p. 24.
Postoperative Studies of Pulmonary Stenosis Without Aortic Overriding. G. Ekstrom, A. Lundberg, and T. Moller.—p. 32.
Experimental Approach to the Pathogenesis of Retrolental Fibroplasia: V. The Influence of the State of Nutrition on Oxygen-Induced Changes in the Mouse Eye. B. Hellstrom.—p. 43.
A Comparison of Hemoglobin and Erythrocyte Values in the First-Born and the Second-Born Twin, and in the First, Second and Third Triplet During the Neonatal Period. M. Seip.—p 58.
*Incidence and Significance of Heart Mumurs in Newborn Infants. A. Gyllensward.—p. 63.
On the Effectiveness of Our Pancreatic Enzyme Preparations: A Study of Fat and Protein Absorption and of the Total Amount of Faeces. S. B. Jensen, and M. Schneidelbach.—p. 70.
Evidence of the Presence of a Pitressin-Like Substance in the Tissue Fluids in Nephrosis. H. E. C. Wilson and A. Muirhead.—p. 77.
Children Chronically Diseased. G. Herlitz and B. Redin.—p. 85.
Cortisone Treatment in Vitamin D Intoxication. J. Winberg and R. Zetterstrom.—p. 96.

Incidence and Significance of Heart Murmurs in Newborn Infants.—A group of 11,645 newly born infants were followed to find the incidence and prognosis of heart murmurs. A total of 58 (0.5%) had a murmur during the first week of life. Of those almost half (28) had no murmur by one year of age. Most of these disappeared in the first 6 weeks of life. Of the remaining infants 16 died with obvious heart disease by two years of age, 11 were living but with other signs of congenital heart lesions, and 3 were felt to have functional murmur. The author's conclusion is that one should not inform the mother of any systolic heart murmur unaccompanied by other evidence of heart disease unless it persists beyond three months.

American Heart Journal, St. Louis

51:1-164 (Jan.) 1956

Sanifort's "Observationes," Chapter 1, Concerning a Very Rare Disease of the Heart. L. R. Bennett.—p. 2.

51:165-324 (Feb.) 1956.

Selective Phonocardiography. A. A. Luissada, L. Richmond, and C. Aravanis.—p. 21.
*Eisenmenger's Complex: A Clinical and Pathologic Study of 4 Cases. J. Espino-Vela and L. A. Mata.—p. 284.
Evidence for Heart Damage in Association with Systemic Hypothermia in Dogs. H. S. Samuli Sarajas.—p. 298.
Aneurysm of Right Sinus of Valsalva with Rupture into Right Atrium and into the Right Ventricle. L. Feldman, J. Friedlander, Robert Dillon, and Richard Wallyn.—p. 314.

51:325-486 (March) 1956

Hydrodynamics in Ventricular Septal Defects. P. Brostoff and S. Rodbard.—p. 325.
*The Relationship Between the Pressure Sustained by the Various Cardiac Valves and the Relative Frequency of Their Involvement in Rheumatic Fever. D. E. Tyler.—p. 415.
Effect of Quinidine on the Ventricular Complex of the Electrocardiogram with Special Reference to the Duration of the Q-T Interval. T. O. Cheng, G. C. Sutton, P. Swisher, and D. C. Sutton.—p. 417.
Ruptured Congenital Aneurysm of the Sinus of Valsalva. T. K. Lin, E. Crockett, and E. G. Dimond.—p. 445.

51:487-646 (April) 1956

* A Study of C-Reactive Protein in the Serum of Patients with Congestive Heart Failure, K. Elster, E. Braunwald, and H. F. Wood.—p. 533.
Left-to-Right Extracardiac Shunts in the Presence of Pulmonary Stenosis. D. Bowers, H. J. C. San, and Howard B. Burchell.—p. 568.
A Clinical Evaluation of Acetyl-Digitoxin. R. B. Crouch, M. R. Hejtmancik, and G. R. Herrmann.—p. 609.
Heart Involvement in Progressive Muscular Dystrophy. A. A. Berenbaum and W. Horowitz.—p. 622.
Benign Idiopathic Pericarditis. J. D. E. Price, J. L. Hutchinson, and E. A. S. Reid.—p. 628.
Hematoma of the Interatrial Septum. J. L. Orbison and F. K. Mostofi.—p. 636.

Eisenmenger's Complex.—The authors note the rarity of the Eisenmenger complex, there having been only 6 documented cases in a series of 1500 cases of congenital heart disease at the National Institute of Cardiology of Mexico. The rarity of the condition

plus both the clinical and amatomic similarity of the complex to ventricular septal defect make an antemortem diagnosis of Eisenmenger complex extremely difficult. In addition, bizarre forms of the Eisenmenger complex exist producing physical signs which make the diagnosis even more difficult.

The four cases presented were all atypical forms of the classical Eisenmenger complex. The first of these, in addition to having a ventricular septal defect with biventricular origin of the aorta, was complicated by a fenestrated aortic cusp producing aortic insufficiency. In addition there was a right-sided aorta. The presence of systolic and diastolic thrills and murmurs with a wide pulse pressure led to the erroneous diagnosis of patent ductus arteriosus. The authors point out the patent ductus arteriosus is rarely associated with a right aortic arch and the presence of this anomaly should lead one to suspect a diagnosis other than patent ductus arteriosus.

The second case was atypical in that there was complete dextropostion of the aorta without transposition. Despite the fact that the aorta originated entirely from the right vertricle, visible cyanosis occurred only terminally, indicating that the significant factor in the production of cyanosis is not the biventricular origin of the aorta but the adequacy of pulmonary blood flow.

The third and fourth cases were unique in that in the former the septal leaflet of the tricuspid valve was firmly attached to and completely occluded the ventricular septal defect, while in the latter case the septal leaflet of the tricuspid valve partially occluded the ventricular septal defect. In both the aorta was thought to be dextroposed. In Case 3, there was, in addition, aortic stenosis. Cases 1 and 2 had changes in the pulmonary vascular bed commonly associated with pulmonary hypertension, while Case 3, in whom the ventricular septal defect was sealed so that, although the aorta was dextroposed, it did not have a biventricular origin, had a normal pulmonary vascular bed. The authors consider this as good evidence supporting the concept that the pulmonary vascular changes in Eisenmenger complex are not congenital in origin but are the result of pulmonary hypertension and increased pulmonary blood flow secondary to the altered hemodynamics of the right ventricle resulting from the biventricular origin of the aorta.

The Relationship Between the Pressure Sustained by the Various Cardiac Valves and the Relative Frequency of Their Involvement in Rheumatic Fever.—The pressure sustained by the various heart valves has been thought possibly to be a factor in the localization of rheumatic vascular lesions. The author expands this concept and points out, from a review of four series of patients, that the distribution of rheumatic valvular lesions is approximately proportional to the pressure sustained by each of the valves. In order of decreasing pressure and rheumatic involvement sustained are the mitral, aortic, tricuspid and pulmonary valves.

A Study of C-Reactive Protein in the Serum of Patients with Congestive Heart Failure.—Serial determinations of C-reactive protein were done on 40 patients manifesting cardiac failure to determine if congestive failure alone might result in the appearance of C-reactive protein in the serum. The primary cardiovascular diseases resulting in congestive failure included rheumatic heart disease, active and inactive, subacute bacterial endocarditis, constrictive pericarditis, hypertensive and arteriosclerotic heart disease, arteriosclerotic heart disease with myocardial infarction, and syphilitic heart disease. Of the 40 patients studied, 30 had C-reactive protein in their serum at some time during the episode of congestive cardiac failure. In 23 of these patients there was no detectable disease process other than the congestive failure to which the presence of the C-reactive protein could be attributed. In those patients in whom C-reactive protein was present, the congestive heart failure appeared to be severer, and the abnormal protein disappeared from the serum of 16 patients following recovery from heart failure. In 10 patients in whom congestive failure was stationary, single determinations of C-reactive protein were negative in all. The factors responsible for the appearance of C-reactive protein in congestive failure remain a matter of speculation. The authors conclude that the presence of C-reactive protein in the serum of patients with congestive heart failure limits the use of this test as a measure of rheumatic activity in acute and chronic rheumatic fever and as a measure of necrosis in acute myocardial infarction.

The American Journal of Medicine, New York
20:159-316 (Feb.) 1956

*Relationship of Immune Response to Group A Streptococci to the Course of Acute, Chronic and Recurrent Rheumatic Fever. G. H. Stollerman, A. J. Lewis, I. Schultz, and A. Taranta.—p. 163.
*Relationship of Sydenham's Chorea to Infection with Group A Streptococci. A. Taranta and G. H. Stollerman.—p. 170.
Epidemiologic Studies on Antibiotic-Resistant Strains of Micrococcus Pyogenes. R. I. Wise, C. Cranny, and W. W. Spink.—p. 176.
Allergic Reactions in Sites Recurrently Infected with Hemolytic Streptococcus. F. A. Stevens.—p. 185.
Splenomegaly in Sickle Cell Anemia. R. J. Watson, H. C. Lightman, and H. D. Shapiro—p. 196.
The Porphyrins and Porphyria: A Review of 81 Cases. W. J. Martin and F. J. Heck.—p. 239.
Types and Distribution of Antibodies. W. J. Kuhns.—p. 251.
Diffuse Lymphosarcomatosis of the Central Nervous System Simulating Infectious Polyneuritis. R. E. Clausen Jr., A. F. Lincoln, and H. K. Silberman.—p. 292.
Familial Non-Hemolytic Icterus. W. G. Baroody and R. T. Shugart.—p. 314.

Relationship of Immune Response to Group A Streptococci to the Course of Acute, Chronic and Recurrent Rheumatic Fever.—The relationship of the natural course of rheumatic fever to the occurrence of streptococcic infection has been evaluated by means of antistreptolysin, antihyaluronidase, and antistreptokinase titers in 580 patients. Elevated levels for one or more of these three antibodies can be found in 95% of the cases of acute rheumatic fever within two months of onset, whereas any one of the antibody studies will result in only 60% to 70% elevated levels. Over the course of 12 months, the antibody titers fall so that only 20% remain elevated a year after the onset of rheumatic fever, regardless of whether the disease occurred as an acute episode or as a chronic state. This evidence suggests that persistence of the Streptococcus is not the cause for the chronic state. However, of the 580 cases studied, in 95.7% the rheumatic process was clinically arrested within six months of the onset. After the cessation of suppressive treatment with acetylsalicylic acid (Aspirin) or cortisone, all exacerbations of the rheumatic process which were unassociated with streptococcal infection, as demonstrated by negative throat cultures and no antibody rise, occurred within two months. All exacerbations more than two months after the cessation of therapy were associated with antibody rises. This study therefore underscores the importance of antistreptococcal prophylaxis in the prevention of recurrences of rheumatic fever. It also demonstrates the unreliability of antistreptococcic antibodies in determining the prognosis of rheumatic fever.

The Relationship of Sydenham's Chorea to Infection with Group A Streptococci.—Sydenham's chorea is known to occur simultaneously with polyarthritis infrequently. Furthermore the peak seasonal incidence of chorea is in June, whereas that of rheumatic fever falls in April. In an attempt to explain these facts, Taranta and Stollerman analyzed streptococcal antibodies in the sera of patients with "pure chorea" and those with chorea associated with other signs of rheumatic fever. In the latter group were 10 patients in whom chorea developed two to seven months following the initial manifestations of rheumatic fever. During the interval between the initial rheumatic signs and the chorea, repeated throat cultures failed to demonstrate an intercurrent streptococcic infection and antistreptococcal antibodies did not rise. A review of cases in which chorea and carditis occurred together indicated that the carditis had always been present when the chorea developed. Study of the "pure chorea" group demonstrated that the earlier after the onset of the illness that A.S.O. titers were drawn, the more likely they were to be elevated; also the incidence of elevated A.S.O. titers within one month of the onset of pure chorea was almost identical to that observed in rheumatic fever patients studied two months after the onset of their illness. The authors suggest therefore that all Sydenham's chorea is causally related to the antecedent streptococcic infection but that there is a longer "lag period" following the streptococcic infection than occurs with polyarthritis or carditis. A similar lengthy "lag period" has been observed with erythema marginatum, a disorder which also may occur either in an isolated form or as a late rheumatic finding. These studies suggest that, since all Sydenham's chorea would appear to be a sequel of streptococcal infection, such chorea should receive antistreptococcal prophylaxis similar to that given rheumatic fever patients.

American Journal of Pathology, Ann Arbor, Mich.

32:1-159 (Jan.-Feb.) 1956

Pneumocystis Infection and Cytomegaly of the Lungs in the Newborn and Adult. H. Hamperi.—p. 1.
*Splenic-Gonadal Fusion. W. G. J. Putschar and W. C. Manion.—p. 15.

Splenic-Gonadal Fusion.—Thirty cases, including four in the current report, of fusion of the spleen with the left gonadal-mesonephric structures have been described in the literature. The anomaly occurs in two forms: in 18 cases a continuous cord-like structure connected the spleen and the gonads, and in 12 the fused structures had lost continuity with the main portion of the spleen and presented as a variant of accessory spleen. Of the former group 15 and of the latter group all 12 were males. In nine instances of the first type the gonads were incompletely descended, as though the cord from the usually normally located spleen prevented normal development. In the second type the accessory spleen was attached to an inguinal or scrotal testis, and symptoms of scrotal enlargement and tenderness were common. Five of the cases in the first group also had peromelus and three of these had micrognathia. It is assumed that the malformations had their origins in the fifth to eighth weeks of fetal life, when the spleen and developing gonads are in close proximity, the extremity buds differentiating, and the mandibular cartilage forming.

The American Review of Tuberculosis and Pulmonary Diseases, New York

73:1-156 (Jan.) 1956

Pneumocystis Infection and Cytomegaly of the Lungs in the Newborn and Adult. H. Hamperi.—p. 1.
*Observations of the Effect of Cortisone in the Treatment of Tuberculous Meningitis. E. L. Kendig Jr., S. H. Choy, and W. H. Johnson.—p. 99.
Streptomycin, Isoniazid, and Para-Aminosalicylic Acid in the Treatment of Pulmonary Tuberculosis. J. A. Wier and others.—p. 117.

Observations on the Effect of Cortisone in the Treatment of Tuberculous Meningitis.—Two cases are reported of infants with tuberculous meningitis who were treated with cortisone after developing signs of block of the cerebrospinal fluid pathways. Both infants were treated with streptomycin, isoniazid, and para-aminosalicylic acid. One patient developed a cerebrospinal fluid protein of 5600 mg/100 ml. in the second month of antitubercular treatment, which fell to 650 mg/100 ml on therapy with 100 mg. (decreasing to 50 mg.) of cortisone daily, only to raise again to 5800 mg/100 ml. on stopping the cortisone. Reinstitution of cortisone (300 mg. daily decreasing to 100 mg.) was associated with a prompt drop of the protein content to only slightly elevated levels by the time of discharge.

The second infant was comatose when cortisone was started but after improving slightly developed decerebrate rigidity and died. The cerebrospinal fluid protein decreased from levels of 240 mg/100 ml. to normal levels at the time of death four months later. A tuberculosis cavity grew rapidly during treatment.

Although only two cases are presented there is suggestive evidence that cortisone may aid in preventing cerebrospinal block. Caution must be exercised regarding any pulmonary lesion.

Bulletin of the Johns Hopkins Hospital, Baltimore

98:1-64 (Jan.) 1956

Studies on the Pathogenesis of Fever: III. Failure to Demonstrate Fever-Producing Substances in the Tissues of Leukopenic Rabbits. I. L. Bennett Jr.—p. 1; IV. Further Observations on the Production of Fever in Rabbits by the Fluid of Sterile Exudates. I. L. Bennett Jr.—p. 7.
*Sexual Incongruities and Psychopathology: The Evidence of Human Hermaphroditism. J. Money, J. C. Hampson, and J. L. Hampson.—p. 43.

98:65-158 (Feb.) 1956

An Electronmicroscopic Study of the Fine Structure of Pulmonary Capillaries and Alveoli of the Mouse: Preliminary Report. H. E. Karrer.—p. 65.
Antibiotics in Experimental Tetanus: In Vitro and In Vivo Studies. A. A. Anwar and T. B. Turner.—p. 85.
*Some Factors Influencing the Formation of L. E. Cells: A Method for Enhancing L. E. Cell Production. W. H. Zinkham and C. L. Conley.—p. 102.
*The Pathology and Pathogenesis of Experimental Anaphylactic Glomerulonephritis in Relation to Human Acute Glomerulonephritis. A. R. Rich.—p. 120.

Sexual Incongruities and Psychopathology.—The authors have, over the past four years, made a thorough sociologic, psychologic, and psychiatric study of 94 juvenile and adult hermaphrodites. These data and their interpretation have formed the basis for several publications, of which this is one. This paper appraises "the psychologic healthiness" of these patients. The authors define psychologic healthiness and three degrees of nonhealthiness. Only one patient is severely nonhealthy and this is a severe mental defective. Notable is the absence of psychosis in the entire group. Sixty-three are rated as healthy and the remaining thirty are evenly divided betwen mild and moderate nonhealthiness. The effects on psychologic healthiness of the variety of hermaphroditism, the age of the patient, reassignment of sex, visible somatic ambisexuality, and the effects of cortisone in female pseudohermaphrodites with hyperadrenocorticism are discussed. The authors point out, as they have in previous publications, that reassignment of sex beyond early infancy despite the person's chromosomal, gonadal, or hormonal sex is extremely conducive to psychologic unhealthiness.

Some Factors Influencing the Formation of L.E. Cells.—Three factors appear to be necessary for the formation of L.E. cells in vitro. These are a "plasma factor" which is evidently a specific substance associated with the gamma globulin fraction of the plasma proteins of many patients with systemic lupus erythematosus, leucocytic nuclear material, and actively phagocytic white blood cells. There is evidence that damaged leucocytes are a particularly good source of the leucocyte nuclear material. The authors base their new technique on this principle, using as the traumatizing agent small glass beads in which the heparinized blood sample is rotated, after which the specimen is rapidly centrifuged and the buffy coat pipetted off, smeared on cover slips, and stained with Wright's stain. The authors have compared this technique with other standard techniques and find it to be superior. In none of 20 normal adults or 132 patients with diseases other than systemic lupus erythematosus (many of whom had other "collagen" diseases) were either L.E. cells or extracellular material noted. In only 3 of 11 cases of known systemic lupus in which the rotated and clotted blood techniques were compared was the latter more successful in demonstrating the L.E. cells. Ten patients were observed who produced only extracellular material but no rosettes or L.E. cells. There is evidence that extracellular material it derived from the nuclei of injured or dead leucocytes under the influence of L.E. plasma factor. Why L.E. cells are not produced in the presence of this extracellular material remains obscure. The authors point out that although this technique appears to be superior to the others mentioned there are still some patients with systemic lupus erythematosus who fail to produce L.E. cells or extracellular material with any currently available technique.

The Pathology and Pathogenesis of Experimental Anaphylactic Glomerulonephritis in Relation to Human Acute Glomerulonephritis.—The production of diffuse glomerulonephritis after a latent period following either single or multiple injections of nontoxic antigen has seemingly been demonstrated by a number of authors, notable among them Dr. Rich. He believes, however, that neither he nor other authors have demonstrated with sufficient clarity whether the experimentally produced hypersensitivity nephritis is comparable to human glomerulonephritis. The author presents a series of elegant photomicrographs indicating that all types and degrees of glomerular lesions which characterize acute glomerulonephritis can be produced experimentally by the above technique. The evidence that the experimental nephritis is the result of an antigen antibody reaction is presented. The mechanisms by which this reaction is brought about remains completely obscure. It also remains obscure why focal nephritis may be produced in one animal and diffuse glomerulonephritis in another. The author likens these reactions to the variability of hypersensitivity response in man (vasomotor rhinitis, gastrointestinal upset, urticaria, purpura, eczema, asthma, etc.) to the same antigen. The evidence that human glomerulonephritis is a hypersensitivity phenomenon is strongly supported by similarity of lesions and experimental hypersensitivity nephritis, but does not constitute final proof. The demonstration by Rammelkamp that some types of Group A streptococci, particularly types 12 and 4, are more nephritogenic than others should help define this point. The mechanisms whereby these strains are more nephritogenic remain unknown but could be due either to production of particular antigen not produced by other strains

of type A streptococci or to the fact that the antigens produced have a greater affinity for glomerular tissues than non-nephritogenic types.

Canadian Medical Association Journal, Montreal

74:1-98 (Jan. 1) 1956

*Combined Immunization from the Viewpoint of the User in the Field. J. M. Mather.—p. 9.
Hereditary Spherocytosis. J. D. Stenstrom and H. S. Ford.—p. 34.
Serum Proteins in Parturient Mother and Newborn: An Electrophoretic Study. J. Sternberg, P. Dagenais-Perusse, and M. Dreyfuss.—p. 49.
Intranasal Encephalomeningocele. F. A. Macneil.—p. 63.

74:99-184 (Jan. 15) 1956

The Diepkloof Nutrition and Health Study on Bantu Boys, South Africa. H. leRiche, A. A. Kinnear, and R. J. Smit.—p. 130.
Review of Foreign Body Endoscopy over a Period of 30 Years. D. H. Ballon.—p. 139.

74:185-252 (Feb. 1) 1956

*Congenital Dysplasia of the Hip-Joint. A. Gibson.—p. 204.
Report on Poliomyelitis from Hamilton General Hospital. W. O. Jackson.—p. 207.

Combined Immunization from the Viewpoint of the User in the Field.—An estimation of the value of any antigen must eventually be judged by its ability to reduce the morbidity and mortality of the disease for which it was used. It is only after some years that this can be observed. The use of combined antigens was practiced in the Canadian armed forces during the last war and has been used since among the civilian population.

The author outlines his experience as director of a public health unit in southern Ontario from 1947 to 1952. The use of combined fluid antigens contributed to a considerable reduction in the frequency of cases of diphtheria, of tetanus, and of whooping cough. In regard to whooping cough, the author notes that the diagnosis is perhaps becoming more difficult and the disease seems to be effecting more school-age children than preschool children, probably as a result of early inoculation.

He notes that during the last war the Schick test indicated that 50% to 55% of the members of the R.C.A.F. were susceptible to diphtheria in contrast to the 70% to 80% of the population that were susceptible in 1935 according to Rosenau.

The inclusion of tetanus antigen in the inoculum is of real advantage in that children may be actively immunized so that subsequent injuries entailing the risk of tetanus can be treated with a booster dose of toxoid rather than with antitoxin. It is of advantage also in those cases where the injury seems minor and no antitoxin is given. The author feels, however, that tetanus is thus becoming a disease of adults only. He urges the need to provide reinforcing doses of pertussis vaccine for school-age groups and to encourage immunization of adults against diphtheria and against tetanus.

Congenital Dysplasia of the Hip-Joint.—The author advises the use of the term "congenital dysplasia" rather than "congenital dislocation of the hip" and discusses the varying degrees of displacement. This lesion occurs in roughly 1 in 1000 persons in America. He quotes the experience among a group of Indians in which the incidence was 6%, suggesting heredity as of notable significance.

He urges that diagnosis be made as early as possible, preferably at birth, and points out that the following observations are important:

1. The folds on the inner side of the thigh may be asymmetrical and the perineum widened.
2. The height of the lower end of the femur above the table when the infant is on its back may be different on the two sides.
3. Abduction of the thighs may differ on the two sides.

Unilateral dislocation is more easily detected than bilateral, and the x-ray is helpful, particularly when the child is at least 6 months of age. In treatment abduction of the hip joints is the important point. He advises plaster splints, Frejka's splint, or a splint designed by Ilfeld which is described. He notes that treatment is more difficult after the child is a year old but not impossible. He raises many questions which are not readily answered and discusses surgical methods of correcting the deformity. He raises the interesting question that if there is little or no functional disability connected with congenital dislocation why trouble to attemp reduction, and he notes that the problem is

social and psychological rather than surgical. If nothing is done, the functional disability is small in amount. If replacement is secured, the psychological outlook may be restored during adolescence, but the functional difficulty may be severe, increasingly so as age advances.

Metabolism; Infant Feeding; Milk and Other Foods

Studies on Water Metabolism of Pyridoxine and Pantothenic Acid Deficient Rats. K. Guggenheim, Endocrinology 55:156 (Aug.) 1954.

These studies demonstrate that rats in a state of pyridoxine or pantothenic acid deficiency show a delayed diuretic response to a water load. A similar phenomenon has already been described in protein- and thiamine-deficient rats. In contrast to these latter nutritional disorders, the water retention in pyridoxine and pantothenate deficiency is not due to an impairment of the ability of the liver to destroy the antidiuretic hormone of the posterior pituitary. Experiments both in vitro and in vivo showed that the livers of rats suffering from pyridoxine and pantothenate deficiency inactivated Pitressin as fast as those of well-nourished controls.

Normal diuresis could be restored by cortisone or ACTH, whereas Doca was without any effect. It may be concluded that the cause of the deranged water metabolism in these two types of nutritional disorders is a lack of production or of secretion of cortisone-like substances, due to an insufficient supply of ACTH.

Jacobsen, Buffalo.

The Activators of Growth and the Correction of Their Disturbance in Children. B. Rondinini, Clin. pediat. 36:163 (March) 1954.

The factors which may disturb growth in children are either intrinsic (hereditary, racial, endocrine, or embryonic) or extrinsic (intrauterine, environmental, acquired pathological, or nutritional. The relative importance of each of these disturbing factors met with in pediatric practice is discussed.

Higgins, Boston.

The Effects of the Feeding of Amino Acids on Amino-Acidemia and Amino-Aciduria in Healthy and in Premature Infants. C. Imperato, S. Lo Bianco, and I. Sala, Lattante 26:489 (Aug.) 1955.

Hydrolyzed protein (Nesmida) in doses of 1 gm. per kilogram was fed to infants eight hours after the last feeding. No consistent findings could be established as to the excretion of amino acids in the urine or as to the levels of amino acids in the blood. In the premature infants there was a greater percentage of retention of the amino acids than in the full-term infants.

Higgins, Boston.

Influence of Type of Feeding on Morbidity and Mortality in Infants. R. Ramos and L. Torres-Marty, Acta pediát. españ. 13:413-420 (June) 1955.

The authors review the cases of 200 infants hospitalized in the Barcelona University Pediatric Service. They make correlations between the morbidity and mortality with the type of feeding, whether maternal, artificial, or mixed. Full details of feeding are given. Their conclusion is that to diminish mortality in the first two years, maternal feeding with supplemental feeding and adequate vitamins is necessary.

Allen, Santa Fe, N. Mex.

Amino-Aciduria in Galactosemia. S. Darling and Ole Mortensen, Acta pædiat. 43:340 (July) 1954.

A case of galactosemia in a 5-month-old infant was studied by paper chromatography. The pronounced amino-aciduria which was present diminished when the patient was placed on a milk-free diet. Amino-aciduria in galactosemia is presumed to be of renal origin.

From the Author's Summary.

Breast of Cow's Milk as Infant Food: Discussion on Methods of Comparison. Gert V. Sydow and Nils Faxen, Acta pædiat. 43:366 (July) 1954.

In order to find out whether breast-milk feeding is superior to artificial foods for infants, one should first make sure that the groups for comparison are identical in all respects other than feeding, e.g., that one group does not get more careful nursing or better social surroundings than the other, that the supply of food is equally free or rationed in both groups, and that the risks of infection are the same in both groups. Such a comparison may best be carried out in a Children's Home where every other child is given collected breast milk and the others artificial food and where all the children are nursed together under equal risks of infection. As an example, a very limited investigation of this kind is described in which the number of days with a rise in temperature was found to be considerably higher in the cow's-milk group than in the breast-milk group.

Newborn

From the Author's Summary.

The Pathogenesis of the So-Called Physiological Jaundice of the Newborn. S. Nordio and I. Fazzi, Lattante 26:129 (March) 1955.

At the time of birth of an infant, the left lobe of the liver is gradually diminishing in size; this involves a degeneration of liver cells. Data are presented as to the relative sizes of the two lobes of the liver during this psysiological change by measurements taken on premature and full-term infants who had died. At birth, there is a change in the circulation of the blood through the liver following the tying off of the umbilical vein and a gradual closing of the duct of Aranzio. These factors seem to account for the so-called physiological jaundice of the newborn infant.

Higgins, Boston.

The Prophylaxis and Treatment of Sepsis in the Newborn and Small Infant. G. Bernardi and F. Teza, Lattante 26:140 (March) 1955.

Over a period of three years, 30 cases of sepsis in premature and small babies have been brought for treatment to the Pediatric Clinic at Perugia. The sepsis was due to staphylococci in 21 cases, to pneumococci in 5, to Escherchiacoli in 1, and to undetermined cause in 3. In 19 cases there were metastatic foci. Of 8 premature infants, five died, of 15 infants under one month of age 5 died and of 7 over one month all recovered. Although with the advent of antibiotics and sulphonamide drugs the therapeutic results have been much better, the occurrence of sepsis in small infants is still a very serious condition.

Higgins, Boston.

Leiner's Disease. B. Eva-Di Giacomo and M. R. Stallone, Lattante 26:347 (May) 1955.

Leiner's disease is a generalized exfoliative seborrheic dematitis and occurs only in infants during the first two months of life. Thirty infants with this condition were treated on the basis that the etiology of the disease was a vitamin deficiency. Each infant received vitamin B_6 or a B complex. The therapeutic results were very satisfactory.

Higgins, Boston.

Convulsions in the Newborn. E. Casado de Frias and A. Minkowski, Acta pediát. españ. 13:389-412 (June) 1955.

The authors discuss convulsions in the newborn infant and give clinical summaries on 19 of their cases. Convulsions represent a serious cerebral lesion, especially if they occur at birth or just following it. The prognosis is very poor if they last more than 24 hours, and treatment should be immediate.

The treatment is repeated lumbar punctures and the use of chloral and Gardanal in adequate doses. Phenergan and chloropromazine were used in some cases.

Frequently the ill effects following these convulsions are not noticed until after a year of age. Others may be obvious almost immediately. Sample EEG tracings are shown.

Acute Contagious Diseases

ALLEN, Santa Fe, N. Mex.

THE BLOOD PROTEINS AND THEIR ELECTROPHORETIC PICTURE DURING INFECTIOUS HEPATITIS. M. POMPONIO, Lattante 26:332 (May) 1955.

Analyses and the electrophoretic picture of the serum proteins are recorded for 10 children during the various stages of infectious jaundice. There was found to be a decrease in the amount of albumin and an increase in the amount of the γ-globulin and sometimes of the β-globulin during the height of the disease. With recovery, the findings reverted back to normal, except in some cases the γ-globulin remained high.

HIGGINS, Boston.

ELECTROPHORETIC CHANGES IN THE SERUM PROTEINS OF CHILDREN DURING THE COURSE OF POLIOMYELITIS. E. LUCINI, Lattante 26:361 (June) 1955.

The total protein and the albumin of the blood sera show a fall, while the α- and γ-globulin contents are increased during the acute phase of poliomyelitis. The severer the infection, the more marked are these changes. The degree of these changes should be of prognostic value.

HIGGINS, Boston.

Acute Infectious Diseases

SHIGELLA INFECTIONS—OBSERVATIONS ON RECOGNITION AND MANAGEMENT. MOSES GROSSMAN, California Med. 82:96 (Feb.) 1955.

In review of 117 cases of Shigella enteritis observed in the isolation division of the San Francisco Hospital, it was noted that the commonest symptoms were high fever, liquid and bloody stools, prostration, irritability, and meningismus. The use of antibiotics did not significantly affect the course of the acute illness but resulted in early elimination of the Shigella organisms from the bowel. "Carriers" were found to be particularly resistant to antibiotic therapy.

The disease is self-limited. In 30 cases the patients recovered with only symptomatic treatment. Management of fluid and electrolyte balance was often an important factor in supportive therapy.

PRYOR, Redwood City, Calif.

POLIOMYELITIS VACCINE: A REPORT ON FIELD TRIALS IN SOUTHERN ALAMEDA COUNTY IN 1954. THOMAS R. PERDUE and JAMES C. MALCOLM, California Med. 83:233-236 (Sept.) 1955.

Southern Alameda County was the only area in California to take part in the 1954 nationwide field trials for testing poliomyelitis vaccine. Besides the contribution made in evaluating the vaccine, other benefits were as follows: (1) Participation contributed to the control of a serious communicable disease. (2) Inoculations of vaccine during the field trials in all probability prevented some cases of paralytic poliomyelitis among children in southern Alameda County. (3) The community became better informed about poliomyelitis and more interested in the local health department. (4) Local physicians had an opportunity to contribute to important research and to give a valuable community service. (5) The staff of the Alameda County Health Department became better informed and better prepared for any future responsibilities in poliomyelitis immunization programs.

Other conclusions reached as a result of participation in the 1954 field trials are that the initial planning of the study was hasty and not sufficiently representative of medical and administrative thinking. If the trials had been planned for 1955 instead of 1954 there would have been sufficient time for research to be completed, for professional information to be assured, and for sound design of study.

PRYOR, Redwood City, Calif.

HOSPITAL EPIDEMIC OF GASTROENTERITIS IN INFANTS DUE TO A SPECIFIC STRAIN OF ESCHERICHIA COLI IN THE LYON AREA. P. MONNET, COURTIEU, and J. GUERIN, Pédiatrie 10:163, 1955.

A hospital epidemic of six cases in children due to Escherichia coli 111 B_4 was studied bacteriologically. The rigid preventive methods used which led to the limitation and termination of the epidemic were pointed out.

GLASER, Baltimore.

THE TREATMENT OF RESPIRATORY INHIBITION IN POLIOMYELITIS: RESULTS OBTAINED IN THE 1952/1953 EPIDEMIC IN COPENHAGEN. H. CASPARIS, Schweiz. med. Wchnschr. 85:132 (Feb. 5) 1955.

During the epidemic of poliomyelitis in Copenhagen, a relatively simple apparatus for artificial respiration was devised. Depending on circumstances, the respiratory mixture can be given by mask or through a tube introduced by tracheotomy. Satisfactory ventilation can be obtained by means of manual artificial respiration by way of the respiratory bag. The disadvantage of the method is the necessity of trained teams. In some cases a modern iron lung is indicated. A number of tests are needed to control the ventilation, such as pH of the blood, CO_2 of arterial and venous blood, and arterial O_2 saturation. Other tests keep track of metabolism of renal function and hemoconcentration to recognize impending shock. The precautions to avoid aspiration and accumulation of secretions are outlined, as well as the indications for artificial respiration. It was possible to reduce the mortality of severe poliomyelitis cases with paralysis of deglutition and respiration from over 80% to below 40%.

AMBERG, Rochester, Minn.

THE EFFICACY OF VACCINATION AGAINST DIPHTHERIA BY ANATOXIN ADMINISTERED BY A "PATCH TEST." M. LA PLACA, E. SUZZI-VALLE, S. MIGLIARESE-MALESANE, and R. CANDIDA, Clin. pediat. 37:101 (Feb.) 1955.

This test involves the placing on the clean dry skin of the chest a pad held in place by adhesive tape and containing diphtheria anatoxin in an oily medium. Tests have been made to show that this procedure is efficacious in restoring the antitoxin titer of the blood sera of persons who had previously received injections. In other words, it acted as a booster shot. This procedure is analogous to the patch test for tuberculin sensitivity.

HIGGINS, Boston.

ISONIAZID IN THE CURE OF TUBERCULOUS MENINGITIS. P. RITOSSA and M. LATO, Clin. pediat. 37:163 (March) 1955.

Isoniazid was the only antibiotic used in the treatment of eight children, ranging from 4 months to 13 years of age, who had proved tuberculous meningitis. Each of the children had a complete recovery, the hospital stay lasting from 3 to 6 months. Over this period a total of 7 to 49 gm. of the drug was given orally and 1.5 to 3.5 gm. intrathecally. The lumbar and the suboccipital routes were both used at each intrathecal treatment. The recommendation is made that in those cases where the patient is seen early in the disease and before marked encephalitis or cranial nervous disturbances have appeared, the treatment of choice is by isoniazid alone.

HIGGINS, Boston.

CAN THE FINDING OF BECLARD'S NUCLEUS BY X-RAY BE OF AID IN THE DIFFERENTIAL DIAGNOSIS BETWEEN PREMATURELY AND CONGENITAL DEBILITY? E. DE TONI, Lattante 26:516 (Aug.) 1955.

The nucleus of Béclard is in the distal epiphysis of the femur. Its presence was detected by x-ray films in 80% of full-term infants with congenital debility and in 46% of premature infants. An absolute differential diagnosis between these two groups of infants cannot be established by the presence or the absence of this nucleus on x-ray films.

HIGGINS, Boston.

THE IMPROVED PROGNOSIS IN WATERHOUSE-FRIDERICHSEN'S SYNDROME. BERNARDO PEREZ MORENO, Acta pediát. españ. 13:245-249 (April) 1955.

The author presents two case histories of children with Waterhouse Friderichsen's syndrome. Both had been exposed to relatives who had epidemic meningococcic meningitis.

The first was not seen early and died, although cortisone and penicillin were used.

The second was treated immediately and not only recovered but recovered rapidly.

The author believes that cortisone with antibiotics are a specific for this syndrome and that the important thing now is the recognition and early treatment of these cases.

ALLEN, Santa Fe, N. Mex.

Viremia in Human Mumps Infection. F. Muller and H. Lippelt, Deutsche med. Wchnschr. 80:80 (Jan. 14) 1955.

From the blood of a boy 11 years of age and a girl 5 years of age mumps virus could be cultured on the first and third days of mumps, respectively.

Amberg, Rochester, *Minn.*

The Antibiotic Treatment of Salmonella Infections in Childhood. F. Graser, Med. Klin. 50:246 (Feb. 11) 1955.

Treatment of a case of Salmonella typhi meningitis not responding well to various antibiotics responded promptly to a combination of chloramphenicol and Aureomycin. In another infant with a meningitis due to Salmonella enteritidis, this combination also proved effective, and also in another infant with a pachymeningitic abscess due to the same organism. This treatment cleared the infection, permitting surgical treatment. In some cases with persistent presence of Salmonella in the feces, the combined treatment was successful. Another case is cited where a cholecystitis due to Salmonella typhi ruptured with a consequent peritonitis which yielded to chloramphenicol and Terramycin, which was given intravenously.

Amberg, Rochester, Minn.

Chronic Infectious Diseases

The Later Status of Children Who Had Been Treated for Tuberculosis by Antibiotics When They Were Under Two Years of Age. B. Rondinini, Clin. pediat. 37:415 (June) 1955.

One hundred eighty-three children with tuberculosis were treated with antibiotics during the years 1948 to 1952, when they were under 2 years of age. Thirty-five of these children died from the tuberculosis (miliary, meningeal, caseous pneumonia). Eighty-five of the others have been followed; ten (11.7%) have during these three to seven years developed a secondary tuberculous infection. Of a group of children who also had tuberculosis in the first two years of life but before 1948 and not treated by antibiotics, only 3.6% had secondary tuberculosis develop over a period of 9 to 15 years.

The conclusion is drawn that infants with tuberculosis not treated by antibiotics develop a higher degree of immunity than infants who have received antibiotics.

Higgins, Boston.

New Aspects of BCG Vaccination. Jesus Villar Salinas, Acta pediát. españ. 13:69-104 (Feb.) 1955.

This is a rather complete study of the use of BCG in Spain since the revision of the methods of use started in 1948.

The international investigation center under WHO in Copenhagen is used for consultation service as needed.

The continued study of the part allergy plays is the only method by which authentic estimates of population affected and the number of population which is immune can be made.

The author outlines some of the areas in which reporting of reactions must be more exact as well as descriptions of reactions. The simple reporting of percentages is not enough.

He concludes that although there is quite a drop in tuberculosis deaths in Spain, it is important to watch the allergic state of the population, especially in age groups most susceptible to the disease. BCG is still a part of the preventive program in Spain.

Allen, Santa Fe, N. Mex.

Bronchial Ascariasis Treated with Terramycin. Antonio Saez Causillas, Acta pediát. españ. 13:167-171, 1955.

The author gives a case history of a one-year-old child who had bronchial ascariasis proved by x-ray and feces study. The chief symptoms were a prolonged irritative spasmodic cough and loss of weight and disturbed sleep.

The ova of Ascarsis lumbricoides and Oxyuris were found in the feces. Treatment with Terramycin was quite successful, with the abundant elimination of parasites of both types and disappearance of the infiltrative hilar lesion on the left lung.

The child had no recurrence and gained back the lost weight and accustomed good disposition within 15 days.

It was necessary of course to make the differential diagnoses between this condition and (1) pertussis, (2) eosinophilic infiltration of Loeffler, (3) neoplastic and cystic processes, and (4) foreign bodies.

ALLEN, Santa Fe, N. Mex.

Diseases of Blood, Heart and Blood Vessels, and Spleen

ROLE OF AUSCULTATION IN DIAGNOSIS OF CONGENITAL HEART DISEASE. J. D. L. REINHOLD and A. S. NADAS, Am. Heart J. 47:405 (March) 1954.

Sixty-four patients with congenital heart disease were studied by means of phonocardiography. The murmurs in aortic stenosis, "isolated" pulmonary valvular stenosis, ventricular septal defect and single ventricle, atrial septal defect, tetralogy of Fallot, and atypical patent ductus arteriosus are described. The authors' careful observations offer a distinct contribution to the direct and differential diagnosis of these lesions.

GIBSON, Chicago.

ABSENCE OF THE LEFT PULMONARY ARTERY. J. S. MCKIM and F. W. WIGGLESWORTH, Am. Heart J. 47:845 (June) 1954.

The authors report the history, physical examination, clinical course, and autopsy findings in three cases of absence of the left pulmonary artery. Two patients had had tetralogy of Fallot and one an Eisenmenger complex. In all three cases there was a right aortic arch. In all three cases an anomalous obliterated vessel was present, running from the left innominate artery to the hilus of the left lung, continuous with patent, normally distributed, elastic intrapulmonary arteries. The closed portion of the vessel was thought to be an obliterated left ductus arteriosus.

The embryology of this anomaly was discussed. Absence of the left pulmonary artery assumes practical importance when surgical procedures involving occlusion of a branch of the main pulmonary artery are contemplated.

GIBSON, Chicago.

PULMONARY VALVULAR STENOSIS WITH INTACT VENTRICULAR SEPTUM: ISOLATED VALVULAR STENOSIS AND VALVULAR STENOSIS AND VALVULAR STENOSIS ASSOCIATED WITH INTERATRIAL SHUNT. S. S. SABIN, M. J. CARSON, J. L. JOHNSON, and C. R. BAKER, Am. Heart J. 48:416-432 (Sept.) 1954.

Twenty-eight cases of pulmonary valvular stenosis were studied. In 12, isolated valvular stenosis was present. In 16, the pulmonary valvular stenosis was associated with atrial septal defect or patent foramen ovale.

Clinical recognition may be fairly easy in the severe cases. The diagnostic features are increasing exertional dyspnea and fatigue with increasing age, together with marked systolic murmur and thrill in the second and third left interspaces and decreased or absent pulmonary second sound. Cyanosis is absent unless there is an interatrial shunt.

In the milder cases, cardiac catheterization and angiocardiography are important in establishing a diagnosis.

GIBSON, Chicago.

ENDOCARDIAL FIBROELASTOSIS. ELMER G. ST. JOHN and THOMAS A. COPE, JR., Am. J. Roentgenol. 74:39-45 (July) 1955.

This article summarizes previous literature on endocardial fibroelastosis and presents two additional cases for discussion. The clinical manifestations of the three types of endocardial fibroelastosis are discussed: (1) the fulminating type, comprising 25% of cases which occur under 6 weeks of age in a previously normal-appearing child and having a survival of only hours or minutes; (2) the acute type, comprising 51% of the cases, occurring between the ages of 6 weeks and 6 months, in a child considered normal prior to the first episode of paroxysmal dyspnea with cyanosis; the survival is less than 4 weeks, with an average of 15 days; (3) the chronic type, in the remaining 24%, it is usually seen in older infants and children, although it occurs occasionally in the first six months of life.

The diagnosis should be suspected radiographically, as 85% show cardiomegally of a globular or diffuse type and 98% show some evidence of left ventricular enlargement. The etiology remains unknown, although it would possibly represent an inherited developmental defect, and the occurrence in siblings has been reported to the degree that it is statistically significant.

ALTMAN, Miami, Fla.

DIRECT VISION INTRACARDIAC SURGICAL CORRECTION OF THE TETRALOGY OF FALLOT, PENTALOGY OF FALLOT, AND PULMONARY ATRESIA DEFECTS. C. WALTON LILLEHEI, MORLEY COHEN, HERBERT E. WARDEN, RAMOND C. READ, JOSEPH B. AUST, RICHARD A. DEWALL, and RICHARD L. VANCO, Ann. Surg. 142:418-445 (Sept.) 1955.

The surgeon's ultimate goal in treating the tetralogy of Fallot type of congenital heart defects should be to restore the circulation to normal. This is accomplished by both closing the ventricular septal defect and removing the pulmonary stenosis, whether valvular or fundibular.

The advent of controlled cross circulation as a successful method for direct-vision intracardiac surgery has made such corrective surgery possible.

The authors report in detail 10 operated-on cases, all of whom were seriously ill with Fallot's tetralogy. Four died and in six excellent results were obtained.

BANTIN, Omaha.

CONGENITAL CARDIAC MALFORMATIONS IN THE NEONATAL PERIOD. WILLIAM B. OBER and THOMAS E. MOORE JR., New England J. Med. 253:271 (Aug.) 1955.

Survey of 100 autopsied cases of newborn infants dying of congenital cardiac malformation representing more than 100,000 live births indicates that the most frequent cardiac malformations causing death within the first month of life are transpositions of the arterial trunks and large defects of the interventricular septum. The latter may be complete (classified as cor biloculare or cor triloculare) or incomplete (classified as septal defect). These observations contrast with the low prevalence of tetralogy of Fallot and patent ductus arteriosus as a cause of death during the first month of life, although these are the commonest varieties of congenital heart disease encountered both in clinical practice and at autopsy.

FROM THE AUTHOR'S SUMMARY.

SERUM CHOLINESTERASE VALUES IN CHILDHOOD IN HEALTH AND DISEASE. VIRGIL R. BLEISCH and HARRY SHWACHMAN, Pediatrics 13:426 (May) 1954.

The Ravin-Tsou-Seligman colorimetric method of determination of serum cholinesterase has been applied in a survey of over 1000 patients with a wide variety of disease states in a children's hospital. The method is simple, reliable, and specific for serum cholinesterase and can be used as a micromethod.

The average value for healthy children and men is 45.1 units, with a range of 33 to 58. There is no variation with age or sex in childhood. The values are depressed during the neonatal period in full-term and in premature babies. In adolescent girls the values are significantly lower than in boys.

The limited diagnostic significance of single abnormal values, whether high or low, is emphasized. However, extremely high levels suggest the diagnosis of the nephrotic snydrome. Serial determinations may afford a very sensitive index of the course of some diseases. This is especially true in liver disease, malignancy, nephrosis, and malnutrition.

FROM THE AUTHOR'S SUMMARY.

BONE AND JOINT CHANGES IN HEMOPHILIA: A LONG-TERM STUDY IN TWELVE NEGRO SUBJECTS J. B. JOHNSON, T. W. DAVIS, and W. H. BULLOCK, Radiology 63:64-71 (July) 1954.

Twelve hemophiliacs from six families were observed over a period of eight years. The most constant radiographic finding in advanced cases was progressive widening and deepening of the intercondylar fossa of the femora. Punched out or cystic dissolutions were the second most frequent abnormality encountered. The authors believe that when these changes are present in a male, a roentgen diagnosis of hemophiliac arthritis should be the first consideration. The diagnosis of hemaphiliac arthritis in the acute or early stages is almost impossible by x-ray examination alone. Age is an important factor in the differential diagnosis, as in hemophilia bone and joint changes almost always occur before the age of 21.

Systic changes, premature closure of epiphysis, overgrowth, and localized cartilaginous destruction with punched out areas of destruction are frequently seen in hemiophiliac arthritis.

ANSPACH, Riverside, Ill.

COARCTATION OF THE AORTA WITH REGRESSION OF RIB NOTCHING FOLLOWING SURGERY. M. D. JONES and H. L. STAINBACH, Radiology 63:248-250 (Aug.) 1954.

Following resection of the narrowed segment of the aorta and end-to-end anastomosis in a 14-year-old boy, there was definite improvement in rib erosion one year later. The author believes that this was the result of the potential for regeneration of bone in this age group and also indicated evidence of an excellent operative result.

ANSPACH, Riverside, Ill.

ANOMALOUS PULMONARY VENOUS DRAINAGE INTO THE LEFT VERTICAL VEIN. BERTRAM LEVIN and CRAIG W. BORDEN, Radiology 63:317-324, 1954.

One of the more frequent aberrations of the pulmonary venous return, consisting of anomalous drainage of the pulmonary veins into the left vertical vein, which leads to the left innominate vein, is described and illustrated on regular chest roentgenograms and/or with a catheter in the vertical vein in four cases varying in age from 3½ to 32 years. Widening of the superior mediastinal shadow on the left due to the prominence of the vertical vein and in some instances enlargement of the superior vena cava (right) are highly characteristic on regular chest roentgenograms. These shadows combined with that produced by the heart are likened to a "figure of eight."

Clinically there are no major intercardiac abnormalities and few symptoms other than mild exertional dyspnea. However, if an appreciable volume of blood is shunted through an anomalous pulmonary vein from the left to right, a history similar to interatrial septal defects can be anticipated.

One case (3½ years old) came to autopsy, other older cases were diagnosed by insertion of a catheter which was passed from the right arm rather than the left. The examination of blood samples aids in establishing the presence or absence of other anomalies.

ANSPACH, Riverside, Ill.

SPLENECTOMY FOR IDIOPATHIC THROMBOCYTOPENIC PURPURA. M. J. SIMPKISS and I. A. B. CATHIE, Great Ormond St. J. (No. 7) pp. 9-13, June, 1954.

Analysis of 44 cases of idiopathic thrombocytopenic purpura showed that there was nothing to indicate which cases will be self-limiting. It was concluded that spenectomy should be done when recurrences have continued for a year. It is noted that splenomegaly is more often absent than present in these cases.

McGUIGAN, Evanston, Ill.

THE USE OF THE FINGER PLETHYSMOGRAPH AS AN AID TO DIAGNOSIS OF PATIENT DUCTUS ARTERIOSUS. R. V. SELLWOOD, Great Ormond St. J. (No. 7) pp. 32-36, June, 1954.

Observations on the volume pulse flow by means of a finger plethysmograph were made in 14 cases of suspected patent ductus arteriosus. It is concluded that this procedure is of some value in the diagnosis of this condition.

McGUIGAN, Exanston, Ill.

CONGENITAL METHAEMOGLOBINEMIA. D. A. J. WILLIAMSON and J. C. BLACK, Great Ormond St. J. (No. 7) pp. 56-61, June, 1954.

Congenital methemoglobinemia was discovered in an infant who was cyanosed for two weeks from birth, thereafter being noted intermittently when the child was cold or crying. Previous hospital studies had failed to show a cause, though the infant was markedly below normal in growth and development. At 11 months cyanosis was marked and retardation was very noticeable. Vein puncture produced chocolate-brown blood, and spectroscopy methylege blue and ascorbic acid, but a year later he had gained no weight and was physically and mentally greatly retarded.

McGUIGAN, Evanston, Ill.

ACUTE TUBULAR NECROSIS WITH ANAEMIA. JOHN WAGNER, Great Ormond St. J. (No. 7) pp. 66-70 (June) 1954.

A case of tubular necrosis is presented in great detail to illustrate the changes that may occur in the various stages of acute tubular necrosis with ultimate recovery. An attempt is made to explain its cause, as well as the relationship of the associated anemia.

McGUIGAN, Evanston, Ill.

Preliminary Report of an Investigation of Foetal Electrocardiography and Foetal Stethography. J. Davis, M. J. Australia 2:501-504 (Sept. 25) 1954.

The authors have devised a method of fetal electrocardiography which gave satisfactory results in a series of 17 patients with pregnancies from 17 weeks to term. Twenty-nine satisfactory cardiograms were obtained in 32 attempts, including those of both twins in two cases. Satisfactory stethograms were obtained in all cases.

McGuigan, Evanston, Ill.

Chronic Fibroelastic Myoendocarditis (Fibroelastosis of the Endocardium). R. Sacrez, L. Fruhling, and C. Adam, Pédiatrie 10:129, 1955.

Thirteen cases of fibroelastosis were observed at the Children's Hospital in Strasbourg between 1947 and 1954. Eleven were under 1 year, the others were 18 months and 8 years, respectively. Pathologically it is believed that the lesion originates in the myocardium and secondarily induces proliferation of the endocradium. The cases can appear as acute forms without interstitial sclerosis, as combinations between acute inflammatory lesions and sclerosing lesions, more chronic forms with predominantly sclerosing lesions in the myocardium, and the one unusual case of late fibroelastosis.

Glaser, Baltimore.

Test of Circulatory Function by the Standing Experiments in Children with Vegetative Dystonia. V. Kaloud, Ann. pædiat. 182:295 (May) 1954.

In order to find circulatory disturbances caused by vegetative imbalance the standing experiment according to Schellong was carried out in 84 patients of the Graz University Children's Hospital, together with registration of blood pressure, pulse, and electrocardiogram. Besides 15 control subjects, there were 12 children with hypotonic, 2 with hypodynamic, and 39 with hypertonic reaction, as well as 6 with mixed forms and 10 patients who did not fit into any of the mentioned groups. The changes typical for each group are emphasized and analyzed in detail. The changes of the ECG during the standing experiment have to be understood chiefly as a sequel of the disordered neurohormonal balance, as can be concluded from comparing investigations after bandaging the legs and during repetition of the test after dihydroergotamin medication.

Finally, some etiological questions of dystonia are discussed, and the importance of subdividing the different types of reaction as valuable aspects for the planning of the treatment can thus be gained.

From the Author's Summary.

Diagnosis and Treatment of Acute Interstitial Myocarditis in Infancy. S. Van Creveld, J. W. C. De Groot, H. A. Ph. Hartog, and Lie Sing Kiem, Ann. paediat. 183:193 (Oct.) 1954.

The diagnosis and treatment of interstitial myocarditis in infants is discussed. Eleven cases were observed in the pediatric clinic of the University of Amsterdam, six of which died. After a short description of the anatomical picture, the clinical syndrome is described. Special attention is paid to the radiological and electrocardiographic findings. The differential diagnosis is discussed. The importance of early diagnosis and administration of digitalis is stressed.

From the Author's Summary.

Cooley's Anemia in Burma. F. Perabo, Helvet. paediat. acta 9:339 (Oct.) 1954.

Two cases of familial thalassemia (Cooley's anemia) in Burma were described. The diagnosis is based on the clinical findings, the typical peripheral blood picture, the enormous erythropoiesis in the bone marrow, the increased bilirubin content of the blood, and the marked bone changes in the x-rays.

From the Author's Summary.

The Modern Aspect of Coagulation from the Clinical Point of View. F. Koller, Schweiz. med. Wchnchr. 84:804 (July 17) 1954.

Hemophilia with its sex-linked inheritance is not caused by a uniform coagulation deficiency. Hemophilia A is distinguished from hemophilia B. For further detail the paper is to be consulted.

Amberg, Rochester, Minn.

THE USE OF THE GLUCOSIDE FROM DIGITALIS LANATA IN PEDIATRICS. L. PERALE, Clin. pediat. 36: 449 (June) 1954.

The glucoside C from Digitalis lanata (Cedilanid) was used in the treatment of 37 children with heart disease. The drug was tolerated very well, and good clinical results were obtained from its use.

HIGGINS, Boston.

CARDIAC DENSOGRAPHY WITH THE CHILD IN THE ORTHOSTATIC POSITION. G. BELLIENI, M. FRANCHI, AND N. BARDELLI, Clin. pediat. 36:521 (July) 1954.

Cardiac densography involves the analysis of the density of the heart shadow either on an x-ray film or on a fluoroscopic screen. The relative density of the various parts of the heart shadow is determined by a photoelectric cell, which analyzes the density at 5 mm. intervals. Also, by holding the photoelectric cell in one position during fluoroscopy, a curve may be obtained showing the filling and emptying of the heart during a single beat or a group of beats. The scanning of the film permits mapping the position and sizes of the left and right auricles, the left ventricle, and the great vessels.

This paper outlines the information to be gained by densography with the patient in the orthostatic or in the left oblique positions. Examination with the patient in the supine position may in some cases offer more or better information in mapping the cardiac shadows.

HIGGINS, Boston.

ACQUIRED METHEMOGLOBINEMIA IN INFANTS. U. PELLEGRINI AND G. MAZZEO, Lattante 25:321 (June) 1954.

The cases of 5 infants, between 18 days and 3 months of age, are reported where methemoglobinemia was manifested by cyanosis and a brownish color of the blood. The cause of the methemoglobinemia was a high concentration of nitrates in the well water used in preparing the babies' formulas. The concentrations of nitrates in the water were 362, 410, 430, 580, and 1030 mg. per liter; there were only traces of nitrites present. In vitro tests showed that sodium nitrite will change fetal hemoglobin into methemoglobin more rapidly than it will change adult hemoglobin.

HIGGINS, Boston.

RADIOLOGICAL FINDINGS OF BONE CHANGES IN CHILDREN WITH LEUKEMIA. P. BRUSA AND L. PARENZAN, Minerva Pediat. 6:184 (March 31) 1954.

Statistics are presented from the cases of 39 children, 2 months to 11 years old, with leukemia. Of these children, 28 were between 2 and 6 years old; 21 were boys and 18, girls. Pallor was present in all 39 cases, fever in 38, hepatomegaly in 35, enlarged lymph nodes in 33, splenomegaly in 29, hemorrhagic manifestations in 23, and bone and joint pains in 14. Ten cases showed a leucopenia (WBC under 5000), and in ten the white blood cell count was in excess of 50,000 Out of the 22 patients receiving a thorough x-ray study, 15 showed bone changes on the films. The more frequent changes were localized osteoporosis, diffuse osteoporosis, osteosclerosis, and the appearance of the line of Baty and Vogt.

HIGGINS, Boston.

THREE CASES OF DREPANOCYTOSIS (SICKLE-CELL ANEMIA) IN GREEK CHILDREN. E. INGLESSI, Minerva pediat. 6:563 (July 31) 1954.

Reports are given of the cases of three children with sickle-cell anemia seen in the Children's Hospital in Athens. They came from three widely separated localities—one from Piraeus, one from the Island of Lesbos, and one from the Peloponesus. This indicates that the disease is more widespread in Greece than only in the previously reported Peloponesian center of petromagula. In each of the three cases, only one parent showed sickle cells; this is unusual, as the disease has been believed to be transmitted only when both parents have sickle cells in their bloods (homozygotic). The suggestion is offered that the recently prevalent nutritional deficiencies among the Greek peoples may have played a factor in the incidence of the disease. The possibility of the mingling of Negro parentage in Greece as a result of the invading African armies in the war of Greek independence in 1821-1827 is discussed.

HIGGINS, Boston.

Changes in the Blood Picture, Especially the Eosinophile Count, Induced by Cisternography. P. Salomone, Minerva pediat. 6:678 (Sept. 15) 1954.

Following air injections for encephalography by cisternal puncture, there was found to be a marked drop in the blood eosinophile count lasting up to 24 hours. The degree and duration of this fall was found to be parallel with a clinical evaluation of the degree and duration of shock experienced by the patient. Eosinophile counts are recommended as having a prognostic value when encephalography is done.

Higgins, Boston.

The Effect of Digitalis on the Mechanisms of Blood Coagulation. G. Granata and C. Lamberti, Minerva pediat. 7:563 (May 5) 1955.

When Cedilanid (lanatoside C), a glucoside from digitalis leaves, was given to 10 well children in the accepted doses to produce digitalization-saturation and then continued in the accepted doses to main digitalization, the coagulation time and the prothrombin activity of the blood were not changed. Another group, of seven children, were given double the accepted dose of Cedilanid to produce the saturation in a shorter time; then the accepted dose was given to maintain digitalization; the coagulation time of the blood was found to have diminished from an average of 3' 12" to 2' 15" when saturation was reached, but was slowly increasing under the maintenance dose to 2' 22"; simultaneously the percentage of prothrombin activity had risen from 90% to 120% and then dropped to 116%.

In view of the desirability of preventing intravascular clotting in cardiac cases, it is advisable not to hurry digitalization.

Higgins, Boston.

Studies as to the Origin of Rheumatic Changes in the Plasma and the Tissues. F. De Mattels, Minerva pediat. 7:574 (May 5) 1955.

Histological studies were made with rabbits which over a period of time (35 days) had received eight injections of horse or beef serum. Various stages of what may be called rheumatic changes were observated on histological examination of the tissues of these animals. The earliest phase was mucoid edema with diffuse histiocytic hyperplasia seen in the spleen and arterial walls. A later stage was accumulation of fibrinoid material and even necrosis with histiocytic macrophagic hyperplasia in various organs, including the thymus, the heart, the arteries, and the spleen.

Higgins, Boston.

The Myelohematic Picture and Some Factors of Coagulation of the Blood of Infants Treated with Chloramphenicol. C. Cipolloni and G. Gelli, Riv. clin. pediat. 53: (Jan.) 1954.

After a review of the literature on serious manifestations of aplastic anemia following therapeutic treatments with chloramphenicol, the authors examined the hematologic picture and some factors concerning blood coagulation in patients suffering from typhus and brucellosis treated with chloramphenicol, as well as in two normal control subjects. The observed hematologic changes are represented by a slight increase of the lymphocyte-neutrophile ratio in the leucocytes formula, by a slight increase of the eosinophiles in the peripheral blood as well as in the marrow blood, and by a very slight delay in the maturation of red and white cells of the marrow. No significant change has been noticed with regard to the hemorrhage time and the coagulation time, the platelet count, the Howell and the Quick-tests, and the heparinic activity of the plasma. The observed hematologic changes decreased after the discontinuance of the chloramphenicol treatment.

From the Author's Summary.

Nuclear Anomaly of Pelger-Huet. Forteza Bover, Calomer Sala, and Marco Orts, Acta pediát. españ. 12:539-546 (June) 1954.

In a routine examination of a school boy, the leucocytic anomaly first described by Pelger Huet was found. No clinical signs of any kind were present. The family tree is given, and 13 out of 24 members examined displayed the same types of unsegmented leucocytes.

Details of the leucocyte formula in various members of the family are given, as well as slides showing the atypical cells.

Allen, Santa Fe, N. Mex.

Clinical Considerations on Fifty-Nine Cases of Congenital Heart Diseases Treated Surgically. Gaston Duffau, Alberto Vignau, and Bernardo Moreno, Rev. chilena pediat. 25:257 (June) 1954.

The clinical symptoms of 59 patients operated on in the Roberto del Rio Hospital between the years 1949 and 1953 with different congenital heart lesions are studied, comparing the preoperative and postoperative findings.

The material comprises 34 cases of persistence of the ductus arteriosus, 13 cases of tetralogy of Fallot, 5 cases of tricuspid atresia, 3 cases of coarctation of the aorta, 1 case of coarctation of the aorta and ductus, 2 cases of pulmonary valvular stenosis, and 1 case of Lutenbacher's syndrome.

From the Authors' Summary.

Clinical Consideration of Sixty-Five Cases of Congenital Heart Disease Treated Surgically. Anrulfo Johow, Alfredo Gentz, Luis Barttlet, Alfredo Cifuentes and Mario Noe, Rev. chilena pediat. 25:262 (June) 1954.

The surgical experience on congenital heart disease obtained in the Surgical Service of the Roberto del Rio Hospital from 1949 to 1953 is shown. During this time 65 patients were operated on, 4 of which were done by Prof. Clarence Crafoord, assisted by hospital's surgeons. Considerations of the anesthesia used in this type of patient and the surgical technique used in 28 cases of ductus arteriosus, 13 cases of tetralogy of Fallot, 6 cases of tricuspid atresia, and 3 cases of coarctation of the aorta are commented on.

From the Authors' Summary.

Erythraemic Myelosis (Di Guglielmo) in an Infant. Ruth Wegelius and Tuomas Peltonen, Acta pædiat. 43:280 (May) 1954.

An infant of 2 months exhibited an anemia, combined with a hyperplastic reaction of the erythropoietic organs. Nucleated red blood cells were found in the peripheral blood, but no reticulocytosis was discovered. The spleen was enlarged. In spite of the hyperplasia of the erythropoietic organs, no sign of increased erythropoiesis could ever be found. The nucleated red cells showed signs of disturbance in the normal course of maturation, mainly evidenced by a persistent basophilia of the cytoplasm and by severe malformations of the nucleus in a later stage of maturation. No antianemic agents had any effect on the anemia, and the infant was kept alive by repeated, continuous blood transfusions. He was also given a course of ACTH with apparent good effect. Splenectomy was performed when the child was in good condition after a course of ACTH and continuous transfusion. After this the child was temporarily in comparatively good health but in no better condition than when receiving continuous blood transfusions. The illness lasted for one year and five months after the child was admitted to the hospital the first time and ended with his death.

From the Authors' Summary.

Idiopatic Interstitial Myocarditis. N. Smit, Maandschr kindergeneesk. 22: 161 (May) 1954.

The author states that though myocarditis may be the result of several causes there still remain cases of unknown origin.

The first case was a girl of 12 months who 6 months before had been treated for humeral osteomyelitis. She now came into hospital with marked tachycardia, grey cyanosis, and a very large heart. The electrocardiogram showed negative T-waves in Leads I and II. She died two weeks after admission. Postmortem examination showed myocardial hypertrophy and Fiedler's myocarditis.

The second case was a girl of 3 years with the same symptoms, but she exhibited during her illness hemiplegia with aphasia, evidently the sequel of intracardiac thrombosis with emboli in the cerebral arteries. This child recovered with digitalis therapy, though some cerebral symptoms remained.

Two other children with isolated myocarditis are described; both died, postmortem examination being refused. In the last case the electrocardiogram showed infranodal tachycardia.

van Creveld, Amsterdam.

Anomalies of the Aortic Arch Causing Stridor and Pulmonary Changes. C. E. van der Hoog, Maandschr. kindergeneesk. 22:218 (July) 1954.

Recurrent infections of the lung should attract attention to the possibility of a vascular ring, even if stridor is not evident.

Two cases of compression of the trachea and esophagus by a vascular ring, formed by a right aortic arch, the left subclavian artery, a ductus arteriosus, and the pulmonary artery

are described. Recurrent pulmonary infections were prominent in both children. Surgical treatment was carried out and consisted in division of the ductus in both patients. It is instructive that the operative results were disappointing: the first child died two months after operation because a lump of bread got stuck in the stenosed part of the esophagus; the second patient had to be readmitted six months after operation with bronchopneumonia. The stenosis of the trachea was unaltered.

VAN CREVELD, Amsterdam.

THE DIAGNOSIS OF ABNORMAL ENTRY OF PULMONARY VEINS. J. H. P. JONXIS and F. BEEKHUIS, Maandschr. kindergeneesk. 22:280 (Aug.) 1954.

The physiology of the abnormal entry of pulmonary veins is discussed. The frequent occurrence of a patent foramen ovale is stressed, which might be due to an increase in pressure in the right auricle. Only if all or nearly all pulmonary veins enter the right auricle does a serious strain on the right heart result. The differential diagnosis with auricular septal defect may be difficult. If the abnormal pulmonary veins are entered by a catheter the diagnosis may be evident. Occasionally even pressures and sampling of blood in the right heart may not prove the diagnosis definitely. Dye-dilution curves may give the final answer for the diagnosis. Methylene blue was used in a 1% solution, together with the reflecto-oxymeter of Brinkman. Typical curves were obtained when the dye was injected in the different cardiac chambers and vessels. If the left auricle was not reached, curves were obtained by injection in the left and right pulmonary artery. The abnormal pulmonary veins usually originate from the right lung. Two deflections are obtained by injection in the right pulmonary artery.

VAN CREVELD, Amsterdam.

PURE RED-CELL APLASTIC ANEMIA TREATED WITH CORTISONE. W. VAN ZEBEN and J. VAN LOO, Maandschr. kindergeneesk. 22:290 (Sept.) 1954.

A case of pure red-cell aplastic anemia in an infant is described. The number of thrombocytes and leucocytes was normal, although the white cells in the bone marrow were predominantly lymphocytes. No cells of the red series were found in the bone marrow. Blood transfusions were necessary every six to eight weeks.

Administration of cortisone was followed by a slight reticulocytosis. When blood transfusions were given until the child had a normal hemoglobin content of the blood, and the dosage of cortisone was increased to 75 mg. daily, a remission of blood and bone marrow occurred. Because of the development of Cushings' snydrome, the treatment with cortisone had to be discontinued, and the child relapsed.

Anthranilic acid, an intermediate product in the metabolic breakdown of tryptophane, was found in the urine.

VAN CREVELD, Amsterdam.

DIFFERENT KINDS OF HEMOGLOBIN. J. J. GOVERS, Maandschr. kindergeneesk. 22:346 (Oct.) 1954.

The different types of human hemoglobin are discussed.

Fetal hemoglobin (hemoglobin F), which is alkali-resistant, is present in children up to 5 months of age in gradually decreasing concentrations. Fetal hemoglobin can always be demonstrated in the blood of older infants, children, and adults in a percentage of 0.5%—1.7% of the total amount of hemoglobin. The demonstration of hemoglobin F, in a concentration of 40%—60%, is of great value in the diagnosis of thalassemia.

Hemoglobin S is found in patients suffering from sickle-cell anemia, and this hemoglobin causes sickling of the cells, in which it is present. The concentration of hemoglobin S in patients with sickle-cell anemia varies between 2% and 23%.

Another type of hemoglobin (hemoglobin III) has been observed in Negroes suffering from a hemolytic syndrome.

FROM THE AUTHORS' SUMMARY.

COARCTATION OF THE AORTA IN INFANTS. J. W. C. DE GROOT and H. A. HARTOG, Nederl. tijdschr. geneesk. 98:543 (Feb. 27) 1954.

After a short discussion of the pathophysiology and anatomy of the coarctation of the aorta, the case reports of five infants below the age of 4 months are described. In each the presenting symptoms are dyspnea, cyanosis, and enlarged heart. The first patient

was successfully operated upon but died 12 hours after operation. Endocardial fibroelastosis of the left ventricle was found as cause of death. The anastomosis was widely patent. The second patient died in heart failure. The ECG showed signs of severe myocardial damage and atrial fibrillation. This child had no murmur. The third patient showed the same symptoms. The lungs were congested. In spite of digitalis administration the child died in heart failure. This child had a complete interruption of the aorta below the left subclavian arterial origin. The ductus arteriosus was widely patent. The following two patients presented a similar picture, with signs of myocardial damage on the ECG. Both died in heart failure and had endocardial fibroelastosis of the left heart. In the first patient an angiocardiogram was made which showed defective empyting of the left ventricle, which was dilated and remained filled with contrast over a period of five seconds. This was suggestive of endocardial fibroelastosis. The femoral arteries could be palpated in some cases, as the lower half of the body was supplied by blood through the patent ductus from the right ventricle. All the anatomical variations of coarctation of the aorta are operable in principle, though diagnosis may be difficult. The possibility of endocardial fibroelastosis should be considered in all cases. It is the opinion of the authors that operation should be attempted as soon as possible, as these children tend to relapse into heart failure.

VAN CREVELD, Amsterdam.

A NEW DIAGNOSTIC AID IN CASES OF ABNORMAL PULMONARY VEINS. J. F. DE VOS, J. L. CHAILLET, J. B. VERHEY, and R. L. J. VAN RUYVEN, Nederl. tijdschr. geneesk. 98:1133-1137, 1954.

The authors report two cases in which it was assumed that one or more pulmonary veins opened up into the right atrium. The course of the catheter or the O_2 concentration of blood samples are not conclusive. Increased pressure and strain of the right heart may not be present. Autopsy and operation revealed in these cases that the diagnosis was wrong.

VAN CREVELD, Amsterdam.

Directory of Pediatric Societies*

INTERNATIONAL

Eighth International Congress of Pediatrics

President: P. Plum Professor, M.D., Domus Medica, Kristianiagade, Copenhagen.

International Union for Child Welfare

President: Mrs. Gordon Morier.
Secretary: Dr. Georges Thélin, 16 rue du Mont Blanc, Geneva, Switzerland.

FOREIGN

Academy of Medicine, Toronto, Section of Paediatrics

Chairman: Dr. Bernard Laski, Toronto.
Secretary: Dr. Crawford Anglin, Toronto.
Place: Academy of Medicine.

Asociacion de Pediatrias Espanoles

President: Dr. Rafael Ramos Fernández.
Vice-Presidents: Dr. Juan Bosch Marin and Dr. Ciriaco Laguna.
Secretary-General: Dr. Luis Navas Migueloa.
Treasurer: Dr. Angel Ballabriga.

Australian Paediatric Association

President: Dr. P. A. Earnshaw, Ballow Chambers, Wickham Terrace, Brisbane. B17.
Honorary Secretary-Treasurer: Dr. D. C. Jackson, 217 Wickham Terrace, Brisbane. B17.
Place: Canberra. Time: Yearly in April.

British Paediatric Association

President: Prof. Stanley Graham.
Honorary Secretary: Dr. Reginald Lightwood, Paediatric Unit, St. Mary's Hospital Medical School, London, W. C. 2.
Honorary Secretary: Dr. Philip Evans, Hospital for Sick Children, Great Ormond St., London W. C. 1.
Place: Windermere. Time: Between Easter and Whitsunday.

Canadian Paediatric Society

President: Dr. J. Harry Ebbs.
Secretary-Treasurer: Dr. J. C. Rathbun, 526 Waterloo St., London, Ont.

Clinical Pediatric Society of Israel

President: Dr. Stanley Levin, Government Hospital, Tiberias.
Vice-Presidents: Dr. Shimon Winter and Dr. George Mundel.
Place: Children's Departments of various hospitals. Time: Last Thursday of the month.

Danish Pediatric Society

President: Dr. A. Rothe-Meyer, Children's Hospital, Fûglebakken, Copenhagen F.
Secretary: Dr. E. Winge Flensborg, Children's Hospital, Martinsvej, Copenhagen V.
Place: Different hospitals. Time: First Wednesday of every month.

Departamento de Pediatria da Associacao Paulista de Medicina

President: Dr. J. Leme da Fonseca.
Secretary: Dr. Joaquim da Costa Marques.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Departmento de Puericultura e Pediatria da Associacao Medica do Parana
President: Dr. Haroldo Beltrao.
Secretary: Dr. Mucio de Abreu Neto.

Deutsche Gesellschaft fur Kinderheilkunde
President: Prof. Dr. med. W. Keller, Freiburg/Brsg., Universitätskinderklinik.
Secretary: Prof. Dr. med. J. Jochims, Lübeck, Städtische Kinderklinik.

Hellenic Society of Pediatrics
President: Dr. A. Androutselli.
Honorary Secretary: Dr. A. Inglessi, 4 Milioni St,, Athens.
Place: Lecture Theater, University of Athens. Time: Last Tuesday of each month, 7 p. m.

Israel Pediatric Society
Chairman: Prof. Sh. Rosenbaum, 26 Bialik St., Tel Aviv.
Secretary: Dr. R. Kochmann, 131 Ben Jehuda Rd., Tel Aviv.
Place: Tel Aviv.

Nederlandse Vereeniging voor Kindergeneeskunde
President: Dr. G. J. Huët, 39 Brediusweg, Bussum.
Secretary: Dr. H. Reerink, c/o Sophia Kinderziekenhuis, 160 Gordelweg, Rotterdam.
Place: Children's Hospital or Pediatric Clinic. Time: Three times a year.

Norsk Pediatrisk Selskap
President: Dr. Henrik Hagelstein, Children's Department, Rikshospitalet, Oslo.
Secretary: Dr. Kare Havard Torp, Children's Department, Ullevål Hospital, Oslo.
Time: Friday, six times a year.

Paediatric Society of Victoria
President: Dr. Arthur J. Day.
Honorary Secretary: Dr. John H. Colebatch.
Place: Royal Children's Hospital, Melbourne. Time: Second Wednesday of each month, February to December, at 8 p.m.

Pediatric Society of New Zealand
President: Dr. Edward J. Cronin, Power Board Bldg., Queen St., Auckland.
Secretary: Dr. J. D. Matthews, 104 Symonds St., Auckland.

Philippine Pediatric Society
President: Dr. Florencio N. Quintos.
Secretary-Treasurer: Dr. Lino Ed. Lim, Manila.
Place: Physician's Club, Dewey Blvd., Manila. Time: Every two months; last Thursday of September, November, January, and March.

Royal Society of Medicine, Section of Paediatrics
President: G. H. Macnab, F.R.C.S.
Honorary Secretaries: Ursula James, M.R.C.P., and Leslie Scott, M.D.
Sectional Editor: D. MacCarthy, M.D.
Place: 1 Wimpole St., London W.1 (correspondence for these honorary officers should be sent to this address). Time: Fourth Friday of each month, 4:15 p.m.

Schweizerische Gesellschaft fur Padiatrie
President: Prof. W. Tobler, Brunnadernrain 11, Bern.
Vice-President: Prof. M. Jaccottet, Av. de Rumine, Lausanne.
Secretary: Dr. J. Haas, Westl. Alpenstrasse 3, Burgdorf.

Sociedad Argentina de Pediatrie
President: Dr. Rudolfo Kreutzer.
Secretary: Dr. Luis M. Cucullu.
Place: Sante Fè 1178, Buenos Aires.

Sociedad Boliviana de Pediatria

President: Dr. Carlos Daza Meruvia.
Secretary: Dr. Cecilio Abela Deheza.
Place: S. C. I. S. P. Bldg. Time: Every Thursday.

Sociedad Chihuahuense de Pediatria

President: Dr. Alfonso Ruiz Escalona.
Secretary: Dr. Armando G. Herrera.
Place: Hospital Infantil del Estado, Chihuahua, Chih., Mexico.

Sociedad Chilena de Dediatria

President: Prof. Dr. Raúl Gantes A.
Secretary-General: Dr. Edmundo Cardemil.
Place: Medical Society, Merced 565, Santiago.

Sociedad Colombiana de Pediatria

President: Dr. Alfonso Vargas Rubiano.
Vice-President: Dr. Darío Gutiérrez Laserna.
Secretary: Dr. Omar García Bustamante.
Treasurer: Dr. Alfonso Gutiérrez Reyes.

Sociedad Cubana de Pediatria

President: Prof. Agustin Castellanos y Gonzales.
Secretary: Dr. Carlos Hernandez Miyares, Apartado 2430, Habana.
Place: Catedra de Clinica Infantil Hospital Nuestra Señora de las Mercedes and Hospital Municipal de Infancia, Habana. Time: 9 p.m., last Wednesday of every month.

Sociedad de Pediatria de Concepcion (Chile)

President: Dr. Daniel Campos, Hospital Clínico Regional, Concepcion.
Secretary: Dr. Obdulia Jiméniz, Hospital Clínico Regional, Concepcion.
Place: Hospital Clinico Regional Concepcion. Time: 7:30 p.m., second Tuesday of every month, April to December, inclusive.

Sociedad de Pediatria del Litoral

President: Dr. Raul Bruera.
Vice-President: Dr. Isidoro Slullitel.
Secretary-General: Dr. Elsa Galimany.

Sociedad de Pediatria y Puericultura del Atlantico

President: Dr. Atilio Marino.
Vice-President: Dr. Helena Uribe de Jimenez.
Secretary-Treasurer: Dr. Hernando Barrios-Angulo.

Sociedade de Pediatria da Bahia

President: Dr. Elysio Pereira de Atbayde.
Secretary: Dr. Eliezer Audiface.

Sociedade de Pediatria de Pernambuco

President: Dr. Antonio Aureliano.
Secretary: Dr. Claudia Figueiredo.

Sociedade de Pediatria do Rio Grande do Sul

President: Dr. Francisco Talaia de Moura.
Secretary: Dr. Enio Pilla.

Sociedade de Puericultura e Pediatria do Maranbao

President: Dr. Odorico Amaral de Mattos.
Secretary: Dr. Joao Mohana.

Sociedade Mineira de Pediatria

President: Dr. Agostinho Fernandes.
Secretary: Dr. Celio Marques Scotti.

Sociedade Portugesa de Pediatria

President: Prof. Dr. Lucio de Almeida.
Vice-President: Dr. Cordeiro Ferreira.
Secretary-General: Prof. Dr. Carlos Salazar de Sousa.
Treasurer: Dr. Mario Cordeiro.
Place: Clinica pediatrica do Hospital D. Estefania, Lisbon. Time: Monthly.

Sociedad Uruguaya de Pediatria

President: Dr. Euclides Peluffo.
Secretary: Dr. Buben Gorlero Bacigalupi.
Place: Av. Agraciada 1464, piso 13, Montevideo.

Sociedad Venezolana de Puericultura y Pediatria

President: Dr. H. Arroyo Parejo.
Vice-President: Dr. Manuel M. Lander.
Secretary: Dr. Guillermo Tovar E., P. O. Box 3122, Caracas.
Treasurer: Dr. Carlos Lares Compos.
Place: Hospital Municipal de Niños "J. M. de los Rios," Caracas. Time: Once a month.

Sociedad Yucateca de Pediatria

President: Dr. Humberto Perez Concha.
Secretary: Dr. Prudencio Ruiz Salazar.
Treasurer: Dr. Jorge Antiveros Andrade.

La Societe de Pediatrie de Montreal

President: Dr. Henri Charbonneau, 3095 Cherbrooke, Montréal.
Secretary: Dr. Edmond Baril, 301 Carré St-Louis, Apt. 1, Montréal.
Time: Second Thursday of each month.

Societe de Pediatrie de Paris

President: Prof. Jean Cathala, 45 rue Scheffer, Paris XVI.
Secretary: Prof. Maurice Lamy, 93 rue de Varenne, Paris VII.
Place: Hôpital des Enfants Malades, 149 rue de Sèvres, Paris XV. Time: 4 p.m., third Tuesday of each month.

Societe de Pediatrie de Quebec

President: Dr. Roland Thibaudeau, 203 des Erables, Québec.
Secretary: Dr. Euclide Dechêne, 312 du Roi, Québec.
Place: Quebec. Time: May and November.

Societa Italiana di Pediatria

President: Prof. Giuseppe Caronia.
Vice-Presidents: Prof. Mario Cotellessa and Prof. Gaetano Salvioli.
Secretary: Prof. Rolando Bulgarelli.

South African Paediatric Association

Chairman: Dr. H. L. Wallace, Durban.
Honorary Secretary-Treasurer: Dr. F. Walt, 126 Trust Buildings, Gardiner St., Durban.

Swedish Association of Pediatrics

President: Prof. Sture Siwe, Lund.
Secretary: Dr. Karl-Axel Melin, Färjestadsvägen 16, Bromma.

Swedish Medical Society, Section for Pediatrics and School Hygiene

President: Docent Justus, Ström, Stockholm.
Secretary: Dr. M. d'Avignon, Pediatric Clinic, Karolinska Sjukhuset, Stockholm 60.
Place: Swedish Medical Society, Klara Östra Kyrkogata 10, Stockholm. Time: Second Friday of each month, except summer.

UNITED STATES

National

American Medical Association, Section on Pediatrics

Chairman: Dr. F. Thomas Mitchell, Memphis.
Vice-Chairman: Dr. Alvah L. Newcomb, Winnetka, Ill.
Secretary: Dr. Wyman C. C. Cole, 3001 W. Grand Blvd., Detroit 2.

American Academy of Pediatrics

President: Dr. Harry Bakwin, 132 E. 71st St., New York 21.
Vice-President: Dr. Edgar E. Martmer, 693 Washington Rd., Grosse Point 30, Mich.
Executive Secretary and Treasurer: Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill.
Place: New York. Time: Oct. 6-12, 1956.

Society for Pediatric Research

President: Dr. Wolf Zuelzer.
Vice-President: Dr. Nathan Talbot.
Secretary-Treasurer: Dr. Sydney S. Gellis, 330 Brookline Ave., Boston.

The American Pediatric Society

President: Dr. Allan M. Butler.
Vice-President: Dr. Bruce Chown.
Secretary-Treasurer: Dr. Aims C. McGuinness, 1427 I St., N. W., Washington 5, D. C.

Sectional

Intermountain Pediatric Society

President: Dr. Warren Tepper, 508 E. S. Temple St., Salt Lake City.
Vice-President: Dr. Stanley Child, 2000 S. 9th E., Salt Lake City.
Secretary-Treasurer: Dr. Merritt H. Egan, 2000 S. 13th E., Salt Lake City.
Place: Ambassador Athletic Club, Salt Lake City. Time: 7 p.m.

New England Pediatric Society

President: Dr. Reuben C. Bates, 122 Waterman St., Providence, R. I.
Vice-President (President-Elect): Dr. Louis K. Diamond, 300 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Harry Shwachman, 300 Longwood Ave., Boston.
Place: Boston, except Spring meeting. Time: Wednesdays, four times a year.

North Pacific Pediatric Society

President: Dr. Carl Ashley, 2455 N. W. Marshall St., Portland, Ore.
Secretary-Treasurer: Dr. S. Gorham Babson, 1107 S. W. 13th St., Portland, Ore.

Northwestern Pediatric Society

President: Dr. A. J. Ouellette, 1530 Larpenteur Ave., St. Paul.
Vice-President: Dr. Elizabeth Lowry, 301 Kenwood Parkway, Minneapolis.
Secretary-Treasurer: Dr. T. C. Papermaster, 215 Doctors' Bldg., Minneapolis.
Place: Minneapolis; St. Paul; Duluth, Minn., and Rochester, Minn. Time: January, April, July, and October.

Rocky Mountain Pediatric Society

President: Dr. Edwin Williams.
Vice-President: Dr. Oliver K. Scott.
Secretary-Treasurer: Dr. John H. Githens, Denver.

Southwestern Pediatric Society

President: Dr. Harold Weatherman, 2001 Fourth Ave., San Diego 1, Calif.
Secretary: Dr. Thomas L. Harris, 436 N. Roxbury Dr., Beverly Hills, Calif.
Place: Jonathan Club of Los Angeles. Time: 6:30 p.m., second Wednesday in January March, May, September, and November.

Western Society for Pediatric Research

President: Dr. Robert Aldrich.
Secretary-Treasurer: Dr. Forrest Adams.

State

Alabama Pediatric Society

President: Dr. David B. Monsky, 748 Adams St., Montgomery 5.
Secretary: Dr. Alice H. Pye, 305 Church St., Montgomery.
Place: Montgomery.

Arizona Pediatric Society

President: Dr. Jacob M. Sobol, 802 N. 2d Ave., Phoenix.
Secretary-Treasurer: Dr. Fred E. Ewart, 24 N. Hibbert St., Mesa.
Time: On call.

California Medical Association, Section on Pediatrics

Chairman: Dr. Moses Grossman, University of California Medical Center, San Francisco 22.
Secretary: Sidney Rosin, 6230 Wilshire Blvd., Los Angeles 17.

Florida State Pediatric Society

President: Dr. Wesley S. Nock, 273 Alhambra Circle, Coral Gables.
Vice-President: Dr. Joel V. McCall Jr., 111 Broadway, Daytona Beach.
Secretary-Treasurer: Dr. Henry G. Morton, 1950 Arlington Ave., Sarasota.

Georgia Pediatric Society

President: Dr. John A. Simpson, Athens.
Secretary: Dr. Harry Lange, 490 Peachtree St., Atlanta.
Place: Savannah. Time: At time of annual state meeting.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. Louis Spekter, Division of Crippled Children, Department of Health, State of Connecticut, Hartford.
Secretary: Dr. Frank E. Roth, 179 Allyn St., Hartford.
Time: With the Connecticut State Medical Society in the spring, with the Connecticut State Clinical Congress in the fall; winter meeting usually in December.

Illinois State Medical Society, Section on Pediatrics

Chairman: Howard R. Miller, 418 Jefferson Bldg., Peoria 2.
Secretary: Harry H. Boyle, 2376 E. 71st St., Chicago 49.

Indiana State Pediatric Society

President: Dr. Harold D. Lynch, Evansville.
Secretary: Dr. L. T. Meiks, Indianapolis.

Iowa Pediatric Society

President: Dr. Arlan F. Harrington, 311 27th St. Dr. S. E., Cedar Rapids.
Vice-President: Dr. James E. Dyson, 3200 University Ave., Des Moines.
Secretary-Treasurer: Dr. Ralph E. Dyson, 3200 University Ave., Des Moines.
Place: Spring meeting in conjunction with the Iowa State Medical Society meeting. Fall meeting in Sept., at University Hospital, Pediatric Dept., Iowa City.

Kansas State Pediatric Society

President: Dr. Bertrand I. Krehbiel, 918 W. 10th St., Topeka.
Secretary: Dr. C. T. Hinshaw, 357 N. Hillside, Wichita.
Time and Place: May, Hutchinson; September, Emporia.

Kentucky Pediatric Society

President: Dr. Alex J. Steigman, University of Louisville School of Medicine, Louisville.
Vice-President: Dr. Daniel B. McIlvoy Jr., Bowling Green.
Secretary-Treasurer: Dr. Selby V. Love, 108 Cannons Lane, Louisville 6.
Place: Louisville. Time: Spring.

Louisiana State Pediatric Society

President: Dr. Jack E. Strange, 3439 Prytania, New Orleans.
Vice-President: Dr. Charles E. Anderson, 1560 Line, Shreveport.

Secretary: Dr. Joseph M. Perret Jr., 2329 S. Carrollton, New Orleans.
Treasurer: Dr. William C. Rivenbark, 1448 Louisiana Ave., New Orleans.
Place: New Orleans. Time: May.

Massachusetts Hospital Association

President: Dr. Philip D. Bonnet, Administrator, Massachusetts Memorial Hospitals, Boston.
Executive Secretary: Henry G. Brickman, 14 Somerset St., Boston 8.

Michigan State Medical Society, Pediatric Section

President: Dr. Horace L. French, 301 Seymour Ave., Lansing.
Secretary: Dr. Park S. Bradshaw, 1014 Jefferson St., Muskegon.

Montana Pediatric Society

President: Dr. Orville M. Moore, 555 Fuller Ave., Helena.
Secretary: Dr. Joseph W. Brinkley, 410 Central Ave., Great Falls.
Place: Variable. Time: Spring and fall.

Nebraska Pediatric Society

President: Dr. Paul Bandroft, Lincoln.
Vice-President: Dr. Charles Tompkins.
Secretary-Treasurer: Dr. A. J. Lombardo, 401 Aquila Ct., Omaha.
Place: Children's Memorial Hospital. Time: 6 p.m., dinner, third Thursday of each month.

New Hampshire Pediatric Society

President: Dr. MacLean J. Gill, 1 South St., Concord.
Secretary-Treasurer: Dr. Robert F. Wilson, 113 Locust St., Dover.
Place: Alternately Concord, Hanover, Laconia, and Manchester. Time: Four times a year.

New Mexico Pediatric Society

President: Dr. M. K. Wylder, Suite 14, Medical Arts Sq., Albuquerque.
Secretary: Dr. Ly Werner, Suite 25, Medical Arts Sq., Albuquerque.
Place: Variable. Time: Every two or three months.

North Carolina Pediatric Society

President: Dr. Wilburt C. Davison, Duke Hospital, Durham.
President-Elect: Dr. Charles F. Williams, 817 Hillsboro St., Raleigh.
Secretary: Dr. William H. Davis Jr., 720 W. 5th St., Winston-Salem.

South Carolina Pediatric Society

President: Dr. Walter Moore Hart, 117 W. Cheves St., Florence.
Secretary: Dr. John R. Paul Jr., 82 Rutledge Ave., Charleston.
Place: Columbia, S. C. Time: Second Monday and Tuesday in September.

Tennessee Pediatric Society

President: Dr. O. L. Von Canon, 846 McCallie Ave., Chattanooga.
Secretary: Dr. Oliver W. Hill, 4807 Newcom Ave., Knoxville.

Texas Pediatric Society

President: Dr. M. C. Carlisle, Waco.
President-Elect: Dr. Russell Blattner, Houston.
Secretary: Dr. James N. Walker, Fort Worth.
Treasurer: Dr. Jack M. Woodall, Big Springs.

Virginia Pediatric Society

President: Dr. T. J. Humphries, Roanoke.
Vice-President: Dr. F. R. Hopkins, Lynchburg.
Secretary-Treasurer: Dr. A. P. Booker, Charlottesville.

Wisconsin State Medical Society, Section of Pediatrics

Chairman: Dr. E. H. Pawsat, Fond du Lac.
Vice-Chairman: Dr. Samuel E. Kohn, Milwaukee.
Secretary: Dr. J. R. Schroder, Janesville.

Delegate: Dr. K. J. Winters, Wauwatosa.
Alternate Delegate: Dr. F. Mellencamp, Milwaukee.

Local

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. C. T. J. Dodge, 15457 Euclid Ave., Cleveland 12.
Secretary: Dr. Beulah Wells, 10515 Carnegie Ave., Cleveland 6.
Place: Allen Memorial Medical Library. Time: 8:15 p.m., October, December, February, and March.

Akron Pediatric Society

President: Dr. Joseph M. Ulrich.
Vice-President: Dr. Lewis E. Rector.
Secretary-Treasurer: Dr. Max E. Griffin.
Time: Quarterly.

Baltimore City Medical Society, Pediatric Section

President: Dr. Wilson Grubb, 4 E. 33d St., Baltimore 18.
Secretary: Dr. Gibson J. Wells, 3101 St. Paul St., Baltimore 18.
Place: 1211 Cathedral St., Baltimore 1. Time: 8:30 p.m., second Tuesday in November, January, and March.

Bronx Pediatric Society

President: Dr. Leon Greenspan, 239 Mount Hope Place, New York.
Vice-President: Dr. Harold H. Aaron, 647 W. 207 St., New York.
Secretary-Treasurer: Dr. Jess Diamond, 1900 Grand Concourse, New York.
Place: Morrisania City Hospital. Time: 8:30 p.m., second Wednesday of each month, except June, July, August, and September.

Brooklyn Academy of Pediatrics

President: Dr. Henry Cohen, 1761 E. 19th St.
Secretary: Dr. A. H. Emerson, 7721 Ridge Blvd.
Place: Granada Hotel, Brooklyn. Time: 8:45 p.m., fourth Wednesday of February, March, April, October, and November.

Buffalo Pediatric Society

President: Dr. Norman Bender.
Secretary: Dr. George B. Rosenfeld, 442 Beach Rd.
Treasurer: Dr. Carl A. Stettenbenz.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p.m., first Monday of each month, September to June.

Central Illinois Pediatric Society

President: Dr. Carl E. Sibilsky, 815 First National Bank Bldg., Peoria.
President-Elect: Dr. O. E. Ehrhardt, 200 S. Grand E., Springfield.
Secretary-Treasurer: Dr. Richard E. Dukes, Carle Hospital Clinic, Urbana.
Place: As announced. Time: April and October each year.

Central New York Pediatric Club

President: Dr. Frank Williams, 58 Swan St. S., Albany.
Secretary: Dr. Fred W. Bush, 325 Park Ave., Rochester.
Place: Various cities in New York State; fall meeting jointly with Upper New York State Academy of Pediatrics. Time: Third Tuesday of April and October.

Central Ohio Pediatric Society

President: Dr. O. W. Hosterman, 350 East Broad St., Columbus 15.
Secretary-Treasurer: Dr. John Riepenhoff, 2998 Sullivant Ave., Columbus.
Place: As announced. Time: Third Wednesday of September, November, January, March, and May.

Chicago Pediatric Society

President: Dr. Maxwell P. Borovsky, 30 N. Michigan Ave.
Vice-President: Dr. S. C. Henn, 2376 E. 71st St.
Secretary: Dr. Ralph H. Kunstadter, 664 N. Michigan Ave.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

Cincinnati Pediatric Society

President: Dr. John E. Allen, 3402 Clifton Ave.
Vice-President: Dr. Robert A. Lyon, Children's Hospital.
Secretary-Treasurer: Dr. William D. De Vaux, 7373 Brookcrest Ave.
Place: Children's Hospital, Elland Ave., Cincinnati: Time: On call.

Cleveland Academy of Medicine, Pediatric Section

Chairman: Dr. Robert Hauver, 10515 Carnegie Ave.
Secretary: Dr. William Herman, 10300 Carnegie Ave.

Corpus Christi Pediatric Society

President: Dr. M. Kurzner.
Vice-President: Dr. Jack McKemie.
Secretary-Treasurer: Dr. Hannah B. Woody.
Place: La Louisiane Restaurant. Time: 7:30 p.m., third Wednesday of January, March, May, July, September, and November.

Dade County Pediatric Society

(See Miami Pediatric Society)

Dallas Pediatric Society

President: Dr. Floyd A. Norman, 4325 Cole Ave., Dallas.
Secretary-Treasurer: Dr. Charles L. Smith, 4207 Lemmon Ave., Dallas.
Place: Children's Hospital of Texas. Time: 6:30 p.m., first Thursday in each month.

Des Moines Pediatric Society

President: Dr. Ralph E. Dyson.
Vice-President: Dr. Charlotte Fisk.
Secretary-Treasurer: Dr. Leonard G. Gangeness, 4119 Rollins (12).
Time: Fourth Tuesday of the month, September through May.

Detroit Pediatric Society

President: Dr. Benton M. Hamil, 2799 W. Grand Blvd.
Vice-President: Dr. Glen E. House, 18520 Grand River.
Secretary: Dr. Louis E. Heideman, 20211 Greenfield.
Treasurer: Dr. Charles G. Jennings, 14827 E. Jefferson.
Place: Variable. Time: Five times a year.
Permanent Mailing Address: 5224 St. Antoine (2).

Fort Worth Pediatric Society

President: Dr. M. W. Brous, 921 Eighth Ave.
Secretary-Treasurer: Dr. William D. Diamond, 554 S. Summit.
Place: Variable. Time: 6:30 p.m., third Friday of each month.

Honolulu Pediatric Society

President: Dr. John Peyton, Medical Group, 1133 Punchbowl St.
Recording Secretary: Goonzo Yamashita, 1618 S. King St.
Corresponding Secretary-Treasurer: Dr. H. M. Sexton, Straub Clinic, 1020 Kapiolani St.
Place: At doctors' homes in rotation. Time: 6 p.m., third Thursday of each month.

Houston Pediatric Society

President: Dr. Fred M. Taylor, Baylor University College of Medicine.
Secretary: Dr. William Betts, 4205 Leeland.
Place: River Oaks Country Club. Time: 6:30 p.m., fourth Tuesday of alternate months.

Kansas City Southwest Pediatric Society

President: Dr. Frank Houge, Plaza Medical Bldg., Kansas City, Mo.
Secretary: Dr. S. J. Kranson, Truman Rd. and Ash, Independence, Mo.
Place: University Club, Kansas City, Mo. Time: On call.

Long Beach Pediatric Society

President: Dr. Kenneth Berkaw, 211 Cherry Ave., Long Beach, Calif.
Secretary: Dr. C. W. Latshaw, 3821 Atlantic Ave., Long Beach, Calif.
Place: Victor Hugo Restaurant, 730 E. Broadway. Time: First Tuesday night of every month.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Robert Shirley, 133 S. Lasky Dr., Beverly Hills, Calif.
Vice-President: Dr. Deron Housepian, 960 E. Green St., Pasadena, Calif.
Secretary: Dr. Margaret Jones, 405 Hilgard Ave., University of California School of Medicine at Los Angeles, Los Angeles 24.
Place: Los Angeles County Medical Association Bldg., 1025 Wilshire Blvd., Los Angeles. Time: Second Thursday of alternate months beginning in September.

Louisville Pediatric Society

President: Dr. Owen S. Ogden, Fincastle Bldg.
President-Elect: Dr. J. J. Glaboff.
Secretary-Treasurer: Dr. Jos. W. Fowler.
Place: Variable. Time: Five times a year, as announced.

Medical Society of the County of Kings and Academy of Medicine of Brooklyn, Pediatric Section

President: Bernard Greenberg, 755 Ocean Ave., Brooklyn 26.
Vice-President: Dr. Joseph Pincus, 881 Washington Ave., Brooklyn 25.
Secretary: Dr. Arthur L. Ruby, 1331 E. 19th St., Brooklyn 30.
Treasurer: Dr. David Dragutsky, 179 Marlboro Rd., Brooklyn.
Place: Kings County Medical Society Auditorium, 1313 Bedford Ave., Brooklyn. Time: 8:45 p.m., fourth Monday of January, March, April, October, and November.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. George Maksim, 1418 Good Hope Rd. S. E., Washington 20.
Secretary: Dr. John E. Cassidy, 5402 Connecticut Ave. N.W., Washington.
Place: Medical Society Bldg., 1718 M St. N. W., Washington. Time: Spring and fall.

Memphis Pediatric Society

President: Dr. Clifton W. Woolley, 2448 Poplar Ave.
Vice-President: Dr. Steve H. Turnbull, 848 Adams.
Secretary-Treasurer: Dr. Charles H. Householder, 321 S. Bellevue.
Place: Rotated among four hospitals. Time: 7:30 p.m., second Tuesday of each month.

Miami Pediatric Society

President: Dr. Warren Quillian, 140 Albambra Circle, Coral Gables.
Secretary-Treasurer: Dr. Robert Grayson, 612-71st St., Miami Beach.

Milwaukee Pediatric Society

President: Dr. Kenneth Winters, Wauwatosa, Wis.
Secretary: Dr. James P. Conway, Milwaukee.
Place: Milwaukee University Club. Time: Second Wednesday of February, April, June, and October.

Minneapolis Pediatric Society

President: Dr. Eldon Berglund, 953 Medical Arts Bldg.
Vice-President: Dr. Edward N. Nelson, 3017 Bloomington Ave.
Secretary: Dr. M. E. Craig, 3400 Dakota Ave.
Treasurer: Dr. Norman Sterrie, 4959 Excelsior Blvd.

Mobile Pediatric Society

President: Dr. Daniel Sullivan, 1420 Government St., Mobile, Ala.
Secretary: Dr. Robert O. Harris III, 1514 Government St., Mobile, Ala.
Place: Admiral Semmes Hotel. Time: 7:30 p.m., fourth Thursday of September, November, January, March, and May.

Nashville Pediatric Society

President: Dr. Thomas Weaver, Bennie Dillon Bldg., Nashville, Tenn.
Secretary: Dr. Ethel Walker, 3415 West End Ave., Nashville, Tenn.
Place: Homes of members. Time: Third Thursday of every month.

Nassau Pediatric Society

President: Dr. John P. Eppig, 3096 Northern Blvd., Manhasset, N. Y.
Vice-President: Dr. Ralph M. Burns, Professional Center, Glen Head, N. Y.
Secretary-Treasurer: Dr. David J. Posner, 98 Walcott Rd., Levittown, N. Y.
Place: Felice's Restaurant, Post Ave., Westbury, N. Y. Time: 9:00 p.m., second Monday of October, December, February, April, and June.

New York Academy of Medicine, Section on Pediatrics

Chairman: Dr. Benjamin Kramer, 60 Plaza St., Brooklyn.
Secretary: Dr. Carl H. Smith, 103 E. 84th St.
Place: New York Academy of Medicine, 2 E. 103d St. Time: 8:30 p.m., second Thursday of each month, October to April, inclusive.

Northern California Pediatric Society

President: Dr. Joseph H. Davis, 300 Homer Ave., Palo Alto.
Secretary-Treasurer: Dr. Samuel Hurwitz, 6200 Geary Blvd., San Francisco 21.
Place: San Francisco. Time: Quarterly, as speakers are available.

Northern Ohio Pediatric Society

President: Dr. Earl E. Smith.
President-Elect: Dr. Chauncey Wyckoff.
Secretary-Treasurer: Dr. C. Q. McClelland.

Oklahoma City Pediatric Society

President: Dr. C. M. Bielstein, 301 N. W. 12th St., Oklahoma City.
Secretary: Dr. Louis Frank, 1200 N. Walker St., Oklahoma City.
Place: Oklahoma Club. Time: On call.

Philadelphia Pediatric Society

President: Dr. Elizabeth Kirk Rose, 426 Owen Rd., Wynnewood, Pa.
Secretary: Dr. Robert H. High, 316 Simms St., Philadelphia 16.
Place: College of Physicians, 19 S. 22d St. Time: 8:30 p.m., second Tuesday from October to May, inclusive.

Pittsburgh Pediatric Society

President: Dr. W. W. Briant, 633 Washington Rd.
Vice-President: Dr. Robert R. Macdonald, 448 Brownsville Rd.
Secretary-Treasurer: Dr. Bernard I. Michaels, 3500 Fifth Ave.
Place: Western State Psychiatric Institute and Clinic. Time: October, December, February, and April.

Queens Pediatric Society

President: Dr. Moe Goldstein, 111-32 76th Ave., Forest Hills, N. Y.
Secretary: Dr. John Finnegan, 36-19 Bowne St., Flushing, N. Y.
Place: Seminole Club, 112th St. and 70th Rd., Forest Hills, N. Y. Time: Second Tuesday in October, December, February, and April.

Richmond Pediatric Society

President: Dr. Hobart T. Dougan, 1832 Monument Ave., Richmond 20, Va.
Secretary: Dr. Robert A. Hoffman, 1001 W. Franklin St., Richmond 20, Va.
Place: Medical College Hospital. Time: 8 p.m., third Thursday of each month, except June, July, and August.

San Antonio Pediatric Society

President: Dr. Philip Magrish, 402 Fulton Ave.
Secretary: Dr. Jack M. Wright, 403 Summit Ave.
Time: 7:30 p.m., supper, first Tuesday of each month.

St. Louis Pediatric Society

President: Dr. Alfred S. Schwartz.
Vice-President: Dr. James P. King.
Secretary: Dr. Miriam H. M. Pennoyer, 500 S. Kingshighway Blvd.
Place: Medart's Restaurant. Time: 7 p.m., second Thursday of each month from September to May, inclusive.

Santa Barbara Pediatric Society

President: Dr. Clarence B. Hills, 22B. W. Micheltorena St., Santa Barbara, Calif.
Secretary: Dr. Louise P. Brown, 3017 Foothill Rd., Santa Barbara, Calif.
Place: Varies. Time: Two to three times yearly, on call.

Seattle Pediatric Society

President: Dr. O. William Anderson.
President-Elect: Dr. Robert Tidwell.
Secretary-Treasurer: Dr. James L. Tucker.
Place: College Club. Time: 6:30 p.m., fourth Friday of each month from September to June.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Fred J. Chapin, 101 John St., Bay City.
Secretary-Treasurer: Dr. George H. Lowrey, University Hospital, Ann Arbor.
Place: University Hospital, Ann Arbor.

Waco Pediatric Society

President: Dr. M. C. Carlisle, 1410 Austin Ave.
Secretary: Dr. A. O. Manske.
Place: Children's Clinic, 2524 Washington St. Time: Fourth Tuesday.

Westchester County Medical Society, Pediatric Section

Chairman: Dr. Donald R. Reed, 14 S. Broadway, Irvington, N. Y.
Secretary: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.
Place: The Roger Smith Hotel, White Plains, N. Y. Time: Four dinner meetings a year, November, February, April, and June.

Western Michigan Pediatric Society

President: Dr. A. Morgan Hill, 310 Fulton, E., Grand Rapids.
Secretary: Dr. John C. Montgomery, 1810 Wealthy St., S.E., Grand Rapids.
Place: Two meetings in Grand Rapids, two elsewhere. Time: First Wednesday of October, November, April, and May.

Wichita Pediatric Society

President: Dr. Mary Blood.
Secretary: Dr. R. A. Nelson.
Place: Homes of members. Time: 8:30 p.m., first Thursday, October through May.